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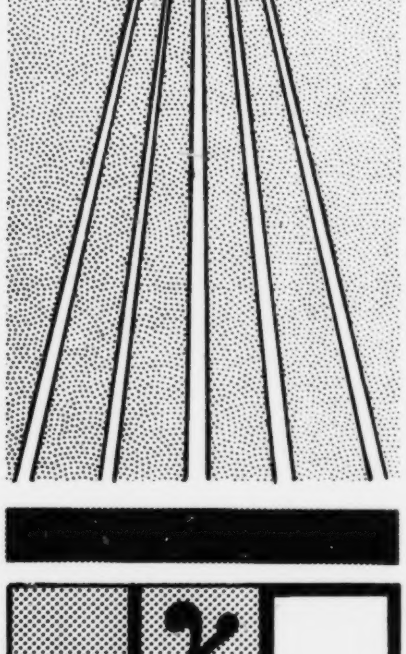

A Training Manual for NUCLEAR MEDICINE TECHNOLOGISTS

A Training Manual for NUCLEAR MEDICINE TECHNOLOGISTS

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

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A Training Manual
for
NUCLEAR MEDICINE TECHNOLOGISTS

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with special acknowledgement to

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For the preparation of Chapter XVII and Appendixes II, III, and IV

OCTOBER 1970

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

Bureau of Radiological Health
Rockville, Maryland 20852

FOREWORD

The Bureau of Radiological Health implements a national program designed to reduce the exposure of man to hazardous ionizing and nonionizing radiation.

Within the Bureau, the Division of Medical Radiation Exposure deals with 1) the reduction of unproductive ionizing radiation exposure of patients, workers, and others exposed by the use of x-rays and other machine-produced ionizing radiation, radioactive materials and radiopharmaceuticals, and 2) the improvement of radiological "systems" and methodology in the healing arts.

The Bureau publishes its findings in Radiological Health Data and Reports (a monthly publication), Public Health Service numbered reports, appropriate scientific journals, and technical report series for the Bureau's divisions, offices, and laboratories.

The technical reports of the Division of Medical Radiation Exposure allow comprehensive and rapid publishing of the results of intramural and contractor projects. The reports are distributed to State and local radiological health program personnel, Bureau technical staff, Bureau advisory committee members, university radiation safety officers, libraries and information services, industry, hospitals, laboratories, schools, the press, and other interested individuals. These reports are also included in the collections of the Library of Congress and the National Technical Information Service (formerly the Clearinghouse for Federal Scientific and Technical Information).

I encourage the readers of these reports to inform the Bureau of any omissions or errors. Your additional comments or requests for further information are also solicited.

John C Villforth

John C. Villforth
Director
Bureau of Radiological Health

PREFACE

~~This~~ manual was prepared for the training program in Nuclear Medicine Technology at the University of Cincinnati. The program was developed under a training grant from the Public Health Service, Bureau of Radiological Health. The purposes of the grant project are to investigate, through pilot programs, various approaches to training Nuclear Medical Technologists and to develop training materials which can be used by others. The program in which this manual is used leads to the Bachelor of Science degree in Medical Technology with a Nuclear Medicine option. The curriculum is as follows:

Freshman Year

English
Inorganic chemistry
Mathematics elective
Foreign language

Sophomore Year

English literature
Organic chemistry (2 quarters)
Biochemistry (1 quarter)
Biology
Social study

Junior Year

Psychology or Philosophy
Literature or Social study
Analytical chemistry (2 quarters)
Bacteriology (1 quarter)
Anatomy & Physiology
Physics

Senior Year

The senior year consists of a 12 month internship in the Radioisotope Laboratory of the Cincinnati General Hospital. The student receives a combination of didactic training, laboratory exercises, and clinical experience. The internship is outlined in the following table:

	Hours per Week			
	Summer	Fall	Winter	Spring
Nuclear Physics & Instrumentation	5*			
Radionuclide Measurements		4* + 2†		
Radiation Protection			4* + 2†	
Tracer Methodology and Radiopharmaceuticals				3*
Clinical Applications of Radionuclides			2*	2*
Hematology and Laboratory Chemistry Lectures		2*	2*	
Technical Evaluation of Nuclear Medicine Procedures	5‡	5‡	5‡	5‡
Clinical Nuclear Medicine and Hematology Practicum	25§	25§	25§	30§

*Didactic lectures
†Laboratory exercises
‡Conference sessions
§Practical experience

This manual is used in teaching the first four courses listed in the internship; i.e., nuclear physics and instrumentation, radionuclide measurements, radiation protection, and tracer methodology and radiopharmaceuticals. It is offered as an addition to the exiguous literature presently available to those who wish to train Nuclear Medical Technologists.

The instructor may find the manual useful as a guideline of topics to be covered in a training program; not necessarily in the order in which they are presented here. For the student, it will serve as a study manual. Some topics, he will find, are covered in adequate depth in the manual, while others will require supplementary reading from the list of suggestions for further reading given at the end of each chapter. These lists are not presented as bibliographies, but rather as additional reading material selected from readily available publications.

The reader will note that stepwise procedures are not included in the manual. Procedures vary from place to place, and the authors recommend that each institution in which this manual is used have available a procedures manual to complement the general information contained herein.

Since college level courses in anatomy and physiology, chemistry, physics, and basic mathematics are prerequisite to the internship in which this manual is used, the fundamentals of these sciences are not included except for the mathematics review in the appendix.

Arve H. Dahl

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Acting Director
Division of Medical Radiation Exposure

Acknowledgement

Much of the material on basic physics and radiation protection was edited from lecture outlines written by members of the Training and Manpower Development Staff of the Bureau of Radiological Health, Public Health Service. The authors also are indebted to Drs. Eugene L. Saenger, James G. Kereiakes, James Mack, Edward Silberstein, and Henry Wellman for reviewing the manuscript.

CONTENTS

Chapter Page

Foreword. III

Preface V

I. Atomic Structure. 1

II. Radioactivity 11

III. Units of Radioactive Decay and the Decay Law. 19

IV. Nuclear Reactions 29

V. Interaction of Radiation with Matter. 37

VI. Principles of Radiation Detection 47

VII. Laboratory Counting Systems 59
I. Integral Counters

VIII. Laboratory Counting Systems 73
II. Pulse Height Analyzers

IX. Medical Radioisotope Scanning Instrumentation 87

X. Nuclear Counting Statistics 105

XI. Principles of In Vitro Counting 117

XII. Principles of In Vivo Counting. 129

XIII. Units of Radiation Exposure and Dose. 141

XIV. Radiation Protection Instrumentation. 145

XV. Principles of Radiation Protection. 153

XVI. Radioactive Tracers and Pharmaceuticals 163

XVII. Clinical Diagnostic Studies 175

Appendixes

I. Mathematics Review 199

II. Radionuclide Activity Schedule 205

III. Dose to Standard Man 213

IV. Erythrocyte and Plasma Volume. 217

CHAPTER I

ATOMIC STRUCTURE

I. STRUCTURE OF THE ATOM

The atom is the simplest unit into which an element can be divided and still retain the properties of the original element. Atoms of all elements are made of three primary subatomic building blocks: electrons, protons, and neutrons. These three primary building blocks are so arranged that the atom may be thought of as consisting of two main parts---the nucleus and the electron cloud. A graphic represenation of several atoms is shown in Figure I-1.

A. The Nucleus

The nucleus is the central portion of the atom and contains two of the three building blocks, the protons and neutrons. Protons and neutrons make up practically all of the mass of the atom. Protons and neutrons are often referred to collectively as nucleons. The nucleus consists of various combinations of protons and neutrons. It is easier to understand the following discussion if these combinations are thought of as being held together by a nuclear force sufficiently great to overcome the coulomb force of repulsion that exists between the positively charged protons. Table I-1 lists the subatomic particles and their physical properties.

Table I.1--Atomic Building Blocks

Unit	Symbol	Relative Mass in Atomic Mass Units	Charge (Electrical)		
			coulomb	esu	relative
proton	p	1.007277	1.6×10^{-19}	4.8×10^{-10}	+1
electron	e	0.0005486	1.6×10^{-19}	4.8×10^{-10}	-1
neutron	n	1.008665	0	0	0

B. The Electron Cloud

The electron cloud surrounds the nuclear portion of the atom and contains the electrons, which are in motion about the nucleus. Since the atom as a whole is electrically neutral the number of electrons in the electron cloud is equal to the number of positive charges (protons), in the nucleus.

The results of various studies[1] of the electron arrangements in atoms indicate that electrons in an atom are grouped into shells each having

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[1] Our knowledge of the electron configurations of atoms has come chiefly from studies of atomic spectra and variation in chemical properties with atomic number.

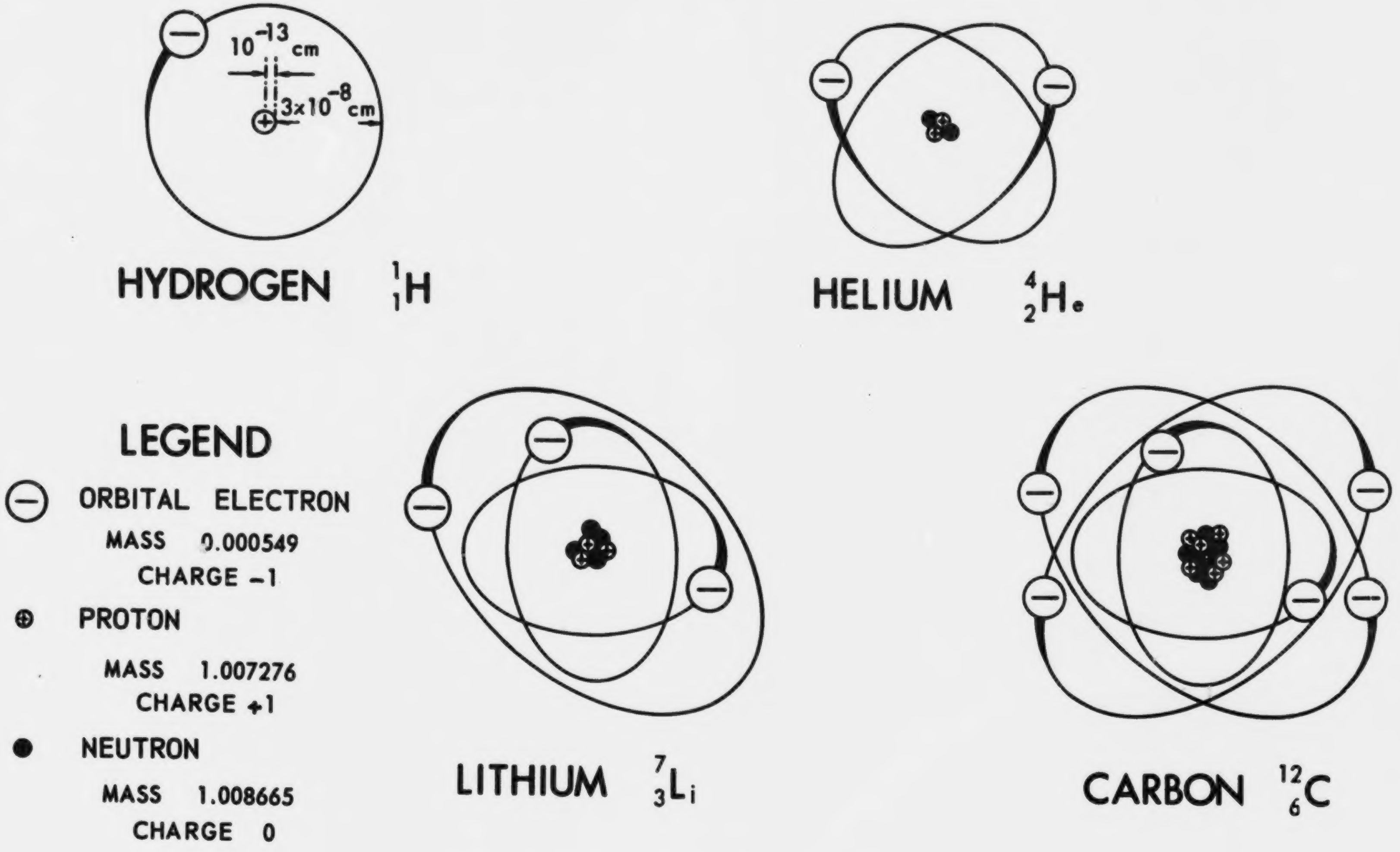
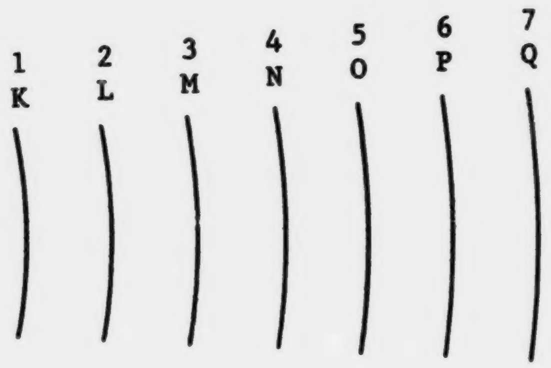

10^{-13} cm
3×10^{-8} cm
HYDROGEN $^{1}_{1}H$
HELIUM $^{4}_{2}He$
LEGEND
ORBITAL ELECTRON
MASS 0.000549
CHARGE -1
PROTON
MASS 1.007276
CHARGE +1
NEUTRON
MASS 1.008665
CHARGE 0
LITHIUM $^{7}_{3}Li$
CARBON $^{12}_{6}C$

Figure I-1.--Atomic Structure

a definite energy and a definite maximum number of electrons. It is customary to visualize electrons of the atom as moving about the nucleus in orbits much as the planets revolve in elliptical paths about the sun. Although this mental image is not entirely accurate, it provides a useful model for understanding the atom. These well-defined orbits (or shells) are often referred to as energy (or quantum) levels, since a definite minimum amount of energy is required to remove an electron from a particular shell. Each shell is denoted by a number in order of decreasing binding energy or, more commonly, by a letter designation from K to Q, as shown below.



The first shell is designated as K, the second as L, the third M, and so on through the alphabet to Q, or the seventh shell, which is the outermost shell found in any of the presently known elements.

II. IONS AND IONIZATION

All atoms in their lowest energy state have the same number of electrons as protons. Consequently, they carry no net electrical charge. When atoms combine to form compounds, the resulting molecule has the same total number of electrons as it does protons, and the molecule is also electrically neutral. Since the electron is the lightest part of the atom and since each electron is not bound as tightly to the nucleus as the protons and neutrons are bound to each other, it is more mobile and can be removed from the atom or molecule by supplying a relatively small amount of energy. As soon as an electron is removed from an atom or molecule, the resulting component has an electric charge because the protons are then in excess of the electrons. After the removal of an electron, the residual atom is called an ion (Figure I-2).

Ions may be charged positively or negatively and may exist in crystals, liquids, or in gases. Positive ions are produced by removing electrons from neutral atoms and molecules, whereas negative ions are created when electrons attach themselves to neutral atoms or molecules. The magnitude of the electrical charge on an ion in terms of electron units, is equal to the number of electrons removed from or added to a neutral atom or molecule. The magnitude of the charge may be calculated by multiplying the number of electrons exchanged (gained or lost) by the charge on each electron in coulombs or electrostatic

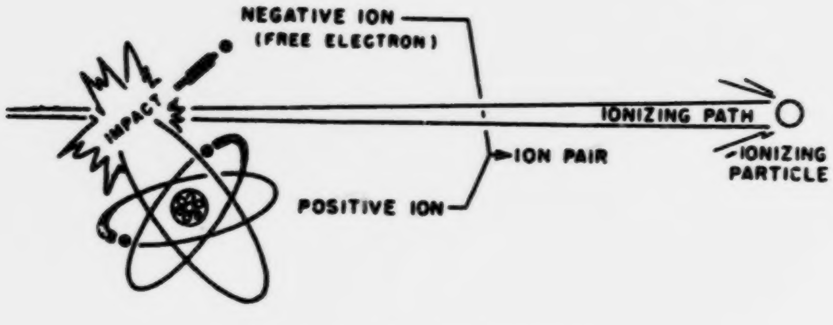


Figure I-2.--Ionization

units. The electron charge is given in Table I-1.

The charge on an ion in terms of electron units is called the valence of the ion. It is common practice to consider a free electron as an ion. Ions are, therefore, defined as free electrons or atoms or groups of atoms carrying a net electrical charge.

Ionization is the process of producing ions. Anything that is capable of removing electrons from (or adding electrons to) neutral atoms or molecules is capable of causing ionization. In radiation physics, ionizing events usually result in the removal of electrons. Consequently, an ionizing event is spoken of as producing an ion pair which consists of the freed electron and the residual positive ion. Ionization is one of the most important results of the interaction of radiation in matter.

III. ATOMIC NOMENCLATURE

Before proceeding further, it will greatly simplify the discussion of the atom to introduce a consistent set of definitions and symbols. A general expression useful for representing a particular isotope is:

$$^{A}_{Z}X$$

A. Chemical Symbols (X)

In the general expression, the X represents the chemical symbol of the element and is used for brevity and convenience. In referring to a specific element, the chemical symbol usually consists of the initial letter[2] (capitalized) in the name of the element, or the initial letter followed by an appropriate second letter. For example, carbon is represented by C, chlorine by Cl, calcium by Ca, oxygen by O, and hydrogen by H.

---

[2] When this system was adopted (1799-1898) the latin names for several metals were in common use. This is reflected in such symbols as Fe (from the Latin ferrum) for iron, Cu (cuprum) for copper, Au (aurum) for gold, Ag (argentum) for silver, Sn (stannum) for tin, and Sb (stibium) for antimony.

B. Atomic Number (Z)

The atomic number (Z) is the number of protons or positive charges in the nucleus.

Since atoms are electrically neutral, the number of electrons in the electron cloud is the same as the number of protons within the nucleus. Each element has an atomic number which is characteristic of the element and is synonymous with the chemical symbol. There are currently over 100 elements, symbols, and atomic numbers. Consequently an element may be designated in any one of the three ways--by name, number, or letter symbol.

C. Mass Number (A)

The A in the general expression ($^{A}_{Z}X$) is the total number of particles (protons and neutrons) in the nucleus and is referred to as the mass number. The mass number is approximately equal to the atomic mass of the atom in atomic mass units.

D. Neutron Number (N) and Isotopes

The number of neutrons in the nucleus is called the neutron number (N) and is equal to the mass number minus the atomic number (A-Z).

When the atoms of an element have the same number of protons but a different number of neutrons, they are said to be isotopes of the element. Such atoms are, in general, indistinguishable chemically. The chemical properties of the isotopes of an element are the same because the chemical properties depend on the number of (orbital) electrons surrounding the nucleus, which in turn is determined by the number of protons in the nucleus.

For example, there are three naturally occurring isotopes of oxygen, namely, $^{16}_{8}O$, $^{17}_{8}O$, and $^{18}_{8}O$. The isotope with a mass number of 16 occurs most abundantly. Another example is hydrogen which has three isotopes, $^{1}_{1}H$, $^{2}_{1}H$, and $^{3}_{1}H$. This element is so significant that its three isotopes are sometimes called by distinct names. The isotope with a mass number of 1 is called hydrogen, the one with A=2 is deuterium, and the third (A=3) is tritium.

IV. UNITS OF NUCLEAR MASS AND ENERGY

A. Atomic Mass Unit (amu)

To appreciate the meaning of the atomic mass unit, consider the relative mass of the particles expressed in grams.

Particle	Weight in grams	Number in one gram
neutron	1.67482×10^{-24}	5.9712×10^{23}
proton	1.67252×10^{-24}	5.0979×10^{23}
electron	9.10908×10^{-28}	1.0979×10^{27}

Since the mass of an individual nuclear particle is very small and, when expressed in grams, involves the use of unwieldy negative exponents, the system of atomic mass units (amu) is employed which uses carbon 12 ($^{12}_{6}C$) as a reference atom. The arbitrary value of 12 mass units has been assigned to carbon 12. The masses of all other atoms are based on a unit which is $\frac{1}{12}$ the mass of the carbon 12 atom. The mass of the lightest isotope of hydrogen is approximately 1 amu.

The mass in grams of an isotope numerically equal to its atomic mass is called a gram-atomic mass. A gram-atomic mass of a substance is also referred to as a mole or equivalent mass of the substance. Since gram-atomic masses are, in magnitude, proportional to the actual masses of the individual atoms, it follows that one mole of any substance contains a definite number of atoms. The number of atoms in one gram-atomic mass is known as Avogadro's number (N_A) and is equal to 6.023×10^{23} atoms/gram-atomic mass.

The mass of any atom in grams can thus be found by dividing the gram atomic mass of the isotope by Avogadro's number. For example, the mass of an atom of carbon 12 is its gram-atomic mass (12 gm) divided by Avogadro's number (N_A).

$$\text{mass of } {}^{12}C = \frac{12 \text{ gm}}{6.023 \times 10^{23}}$$

$$= 1.99 \times 10^{-23} \text{ gm}$$

Since ^{12}C is equal to 12 atomic mass units (amu) the mass of 1 amu would be $\frac{1}{12}$ of the mass of a carbon 12 atom.

$$1 \text{ amu} = \frac{1.99 \times 10^{-23} \text{ gm}/{}^{12}C \text{ atoms}}{12 \text{ amu}/{}^{12}C \text{ atom}}$$

$$1 \text{ amu} = 1.66 \times 10^{-24} \text{ gm.}$$

B. The Erg

To facilitate an understanding of the enormous energy contained in a small mass, consider the energy produced if one amu (1.66×10^{-24} gm) is converted into energy. The conversion can be expressed by Einstein's famous equation relating mass and energy

$$E = mc^2$$

where m is the mass in grams, and c is the velocity of light in cm/sec. Then the energy equivalent (E) of one atomic mass unit is given by

$$E = (1.66 \times 10^{-24}\ \text{gm})\ (3 \times 10^{10}\ \text{cm/sec})^2$$

$$E = 1.49 \times 10^{-3}\ \text{gm-cm}^2/\text{sec}^2.$$

The unit, $\text{gm-cm}^2/\text{sec}^2$, is frequently encountered in physics and is termed the erg, thus:

$$E = 1.49 \times 10^{-3}\ \text{ergs}.$$

C. The Electron Volt

Another convenient unit of energy is the electron volt. An electron volt is defined as the amount of kinetic energy acquired by an electron when it is accelerated in an electric field which is produced by a potential difference of one volt. Since the work done by a difference of potential, V, acting on a charge e, is Ve, and the charge on one electron is 1.6×10^{-19} coulombs, it is possible to calculate as follows:

$$1\ \text{eV} = 1.6 \times 10^{-19}\ \text{coulomb} \times 1\ \text{volt}$$

$$1\ \text{eV} = 1.6 \times 10^{-19}\ \text{joules}$$

Or $$1\ \text{eV} = 1.6 \times 10^{-12}\ \text{ergs}$$

Since the electron volt is a very small amount of energy, it is more commonly expressed in thousands of electron volts (keV) or millions of electron volts (MeV).

1 million electron volts (MeV) = 1,000,000 electron volts

1 kilo-electron volts (keV) = 1,000 electron volts

It is now possible to express the atomic mass unit in MeV.

$$1\ \text{amu} = 1.49 \times 10^{-3}\ \text{ergs, and}$$

$$1\ \text{MeV} = 1.60 \times 10^{-6}\ \text{ergs; therefore,}$$

$$1\ \text{amu} = 931\ \text{MeV}.$$

Therefore, if one amu could be completely transformed into energy, 931 MeV would result. To gain a concept of the magnitude of the electron volt, one million electron volts (MeV) is enough to lift only a milligram weight one millionth of a centimeter.

V. NUCLEAR BINDING ENERGY

The atomic mass of a nuclide can be understood in terms of the masses of its constituent particles and a quantity called the nuclear binding energy. It might be thought that the mass of an atom would be equal to the sum of the masses of the individual particles composing the atom. However, precise measurements of atomic masses show that the mass of an atom is always less than the sum of its constituent particles (as measured in the free state). This difference is called the mass defect and is the amount of mass that would be converted into energy and released (to hold the nucleons together) if an atom were assembled from free neutrons, protons, and electrons. Since this is also the amount of energy required to break up an atom into its component particles, it is therefore called the binding energy of the particular atom. The relationship between binding energy and mass defect is given by Einstein's equation, $E = mc^2$.

The binding energy varies from atom to atom and is usually expressed in terms of the binding energy per nucleon in a particular atom. Figure I-3 shows a plot of the binding energy per nucleon against the mass number (A) for the most stable atoms in nature. Important features of Figure I-3 are: (1) a central region for which the average binding energy is nearly constant ($\approx$8.5 MeV/nucleon); (2) regions at either end of the curve featuring a smaller binding energy per particle (which means a less stable nucleus for both small and large mass numbers); and (3) an unusually large binding energy for small mass numbers having nucleons in multiples of four.

Consider the formation of deuterium as a simple example of the meaning of binding energy. Deuterium is made up of one proton and one neutron in the nucleus, and one orbital electron. The atomic mass of deuterium is 2.014102 (amu). The sum of the masses of its component particles, however, is:

$$\begin{array}{lcr} \text{mass of proton} & = & 1.007277 \\ \text{mass of neutron} & = & 1.008665 \\ \text{mass of electron} & = & \underline{0.000549} \\ \quad\text{Total} & & 2.016491 \end{array}$$

Thus, the mass of the deuterium atom is less than the mass of its component particles by the amount 0.0024 amu. Since 1 amu is equivalent to 931 MeV, the binding energy of the deuterium atom may now be written as:

$$E = 0.0024 \text{ amu} \times 931 \; \frac{\text{MeV}}{\text{amu}} \quad 2.23 \text{ MeV}.$$

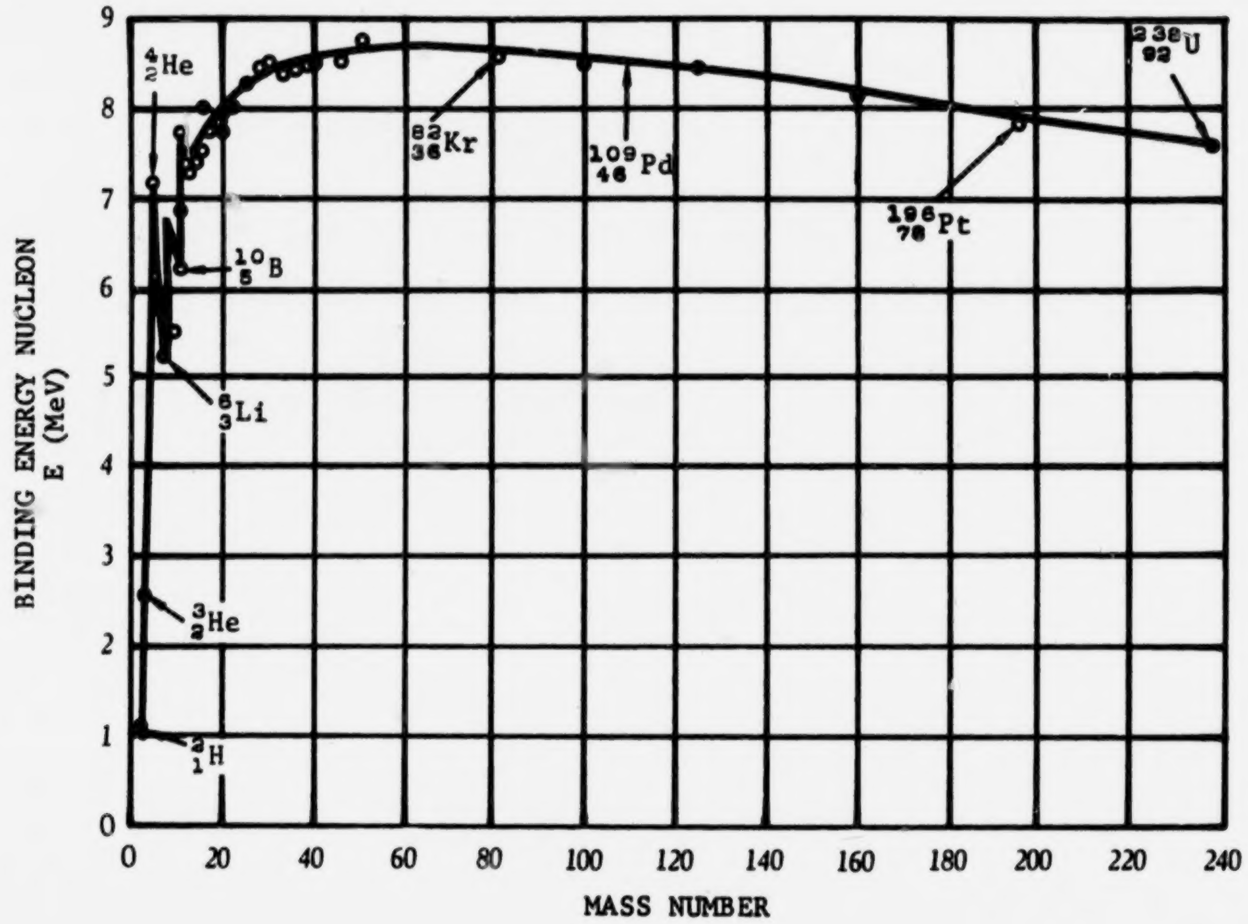


Figure I-3.--Binding Energy vs. Mass Number

The binding energy of the electron is only about 14 eV and is therefore negligible in comparison with 2.23 MeV. Thus, the entire binding energy is essentially that of the two nucleons in the nucleus of the deuterium atom or about 1.11 MeV each.

VI. SUMMARY

The atom is comprised of a nucleus, consisting of neutrons and protons, and orbital electrons. The atomic number (Z) and the atomic mass (A) describe the numbers of these atomic components. There are 92 naturally occurring chemical elements with atomic numbers ranging from 1 to 92. The atomic masses are approximately integral numbers that increase roughly in proportion to the atomic numbers. Most elements have several isotopes differing in mass by one or more mass units from one another. The integral nature of the increments, both in atomic number and mass number, in the periodic table suggest that the nucleus itself is a structure of particles called protons and neutrons having approximately one atomic mass unit each. The protons carry one unit of positive charge and the neutrons are neutral.

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CHAPTER II

RADIOACTIVITY

I. INTRODUCTION

There are certain structural criteria necessary for the nuclei of isotopes of the various elements to exist in a stable state. When these criteria are not met, the nucleus will be unstable and manifest the phenomenon of radioactivity. Radioactivity refers to the processes by which nuclei spontaneously decay or disintegrate by one or more discrete energy steps or transitions until a stable state is reached. The criteria which determine whether a given nucleus is stable or unstable are briefly discussed in the following section of Nuclear Stability.

II. NUCLEAR STABILITY

There are two sets of forces acting on the particles within the nucleus--the relatively long range coulomb forces of repulsion between the positive charges on the protons and the very short range forces between both types of particles. These last forces are only partly understood and no attempt will be made here to discuss them. Suffice to say that the combined effects of these attractive and repulsive forces are such that only certain combinations or ratios of neutrons and protons are stable.

Theoretically, if the coulomb forces were discounted, optimal stability would be achieved within a nucleus when the numbers of protons and neutrons are approximately equal. Such is the situation for the lighter elements in which the coulomb forces, in relation to the short-range forces, are insignificant. These coulomb forces, however, become increasingly significant as the atomic number increases above 20. With significant increases of these repulsive forces within nuclei, intranuclear stability conditions become altered. Consequently, with increasing atomic number, a neutron excess is required in order for a nucleus to be stable.

Thus, for elements which are relatively low in the periodic table (a low atomic number) nuclear stability occurs when the number of neutrons and protons is about equal, or, when the ratio of neutrons to protons (n:p ratio) is approximately equal to unity. As elements increase in Z number above 20, the n:p ratio required for stability gradually increases until $Z = 83$ (bismuth), where the n:p ratio required for stability exceeds 1.5:1. Finally, at the end of the periodic table, above $^{209}_{83}\mathrm{Bi}$, there are no completely stable nuclei. The stability conditions based on n:p ratios are not very critical, and "stability ranges" of n:p ratios exist for any given atomic number or any given mass number. For a given mass number, there may be several stable arrangements of protons and neutrons. For a given atomic number, conditions may vary still more widely so that numerous stable isotopes can occur for a particular element--as many as 10 or 12 stable isotopes for some elements.

The n:p ratio is an over-simplified explanation of the intranuclear criteria leading to nuclear stability. Additional factors involving quantum-mechanical principles and binding energy considerations are needed to further explain stability, but this is beyond the scope of this document.

In summary, nuclear stability is governed by the particular combination and arrangement of neutrons and protons in a given nucleus. If the combination and arrangement of neutrons and protons does not fall within a stable range, then the nucleus is unstable, which is tantamount to saying the nucleus is radioactive. An unstable nucleus attempts to achieve stability by changing its configuration or ratio of neutrons and protons by means of spontaneous disintegration, or radioactive decay.

III. RADIOACTIVITY (Natural and Artificial)

Certain nuclides are found to be unstable as they occur in nature and are therefore called "natural" radionuclides. Others occur as a result of various nuclear reactions brought about by man. The majority of all radionuclides are produced in this manner and are said to be "artificial" radionuclides. The processes involved in the production of artificial radioactivity will be discussed in detail in a subsequent chapter on nuclear reactions.

The first reported evidence of natural radioactivity was by Henry Becquerel in 1896. Becquerel demonstrated that uranium ore would fog or darken a photographic plate which was shielded with opaque paper in much the same manner as x rays. He postulated that the uranium emitted very penetrating rays, similar to x rays. The phenomenon ultimately was called "radioactivity." In time, it was determined that there were many elements beyond the atomic number of lead ($Z = 82$) that showed similar radiating characteristics. After a long and complicated chain of investigations, to which many outstanding physicists contributed, a better understanding of natural radioactivity was gained. The understanding was culminated with the experiments of Rutherford who, in 1903, clearly showed that there were three kinds of radioactive emissions, namely: alpha, (α), beta, (β), and gamma, (γ).

A. Types of Radioactive Emissions

1. Alpha particles (α) are the least penetrating of the three types of radiation and can be absorbed or stopped by a few centimeters of air or a thin piece of paper. Alpha particles are composed of two protons and two neutrons. Hence, they have an electric charge opposite to and exactly twice that of the electrons and a mass number of 4. An alpha particle and the helium nucleus are identical in structure. With a few exceptions, only relatively heavy radioactive nuclides decay by alpha emission.

2. Beta particles (β^-) are negatively charged high-speed electrons. They originate in the nucleus, in contrast with ordinary electrons which

exist in the orbits around the nucleus. In air, they travel several hundred times the distance of alpha particles and require a few millimeters of aluminum to stop them. Beta disintegration occurs most often in nuclei which exhibit a high n:p ratio. The intranuclear effect of a beta emission is that of changing a neutron into a proton thus decreasing the n:p ratio.

3. Gamma rays (γ) like x rays, are electromagnetic radiations which travel with the speed of light. They differ from x rays only in their origins; x rays originate from transitions between electronic energy levels (orbital electron shells), and gamma rays originate from transitions between nuclear energy levels.

Electromagnetic radiations (photons) create wavelike disturbances in space analogous to the disturbance created if a stone is dropped vertically into the center of a pool of water. As the stone strikes the water, a series of crests and troughs are formed which constitute a wave motion as illustrated in Figure II-1. The distance between any two successive crests or troughs is known as the wavelength, which is represented by the Greek letter lambda (λ).

Since all electromagnetic rays travel at the same speed, (3×10^{10} cm/sec or 186,000 miles/sec) in a vacuum, the number of waves (crests) passing a certain point per unit time, or the frequency with which the crests pass the point, will decrease with increasing distance between crests (wavelength). The frequency is represented by the Greek letter nu (ν). The relation between the wavelength λ, the frequency ν, and the velocity of the wave (c) is given by the equation $\nu = c/\lambda$.

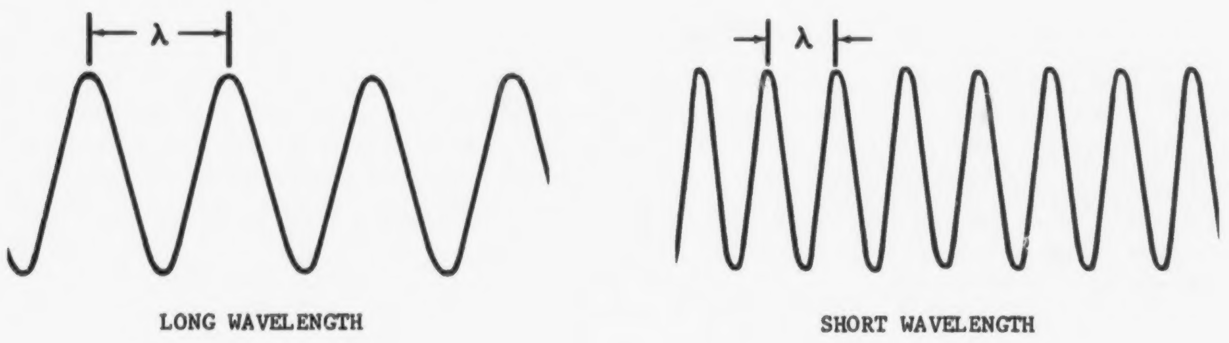

Figure II-1.--Electromagnetic Radiation

The energy of an electromagnetic photon is given by the equation

$$E = h\nu,$$

where: E = energy in MeV

h = Planck's constant = 4.14×10^{-21} MeV sec

ν = frequency (hertz)

Gamma rays occupy a higher energy range on the electromagnetic spectrum than do visible light rays; their energies ranging from a few keV to several MeV.

4. Other modes of decay

The following modes of radioactive decay are associated primarily with artificial radioactivity:

a. Positrons (β^+) are positively charged electrons of nuclear origin. Positron emission occurs only in artificially produced radionuclides, being most likely when the n:p ratio is low. The intranuclear effect of positron emission is that of changing a proton into a neutron, thus increasing the n:p ratio.

b. Orbital electron capture (K-capture) refers to the radioactive decay process whereby the nucleus captures an electron from an orbital shell of the atom. An electron from a higher energy level immediately moves in to fill the vacant position and the excess energy is emitted as a characteristic x-ray photon. The nucleus might conceivably capture an L-shell electron, but K-electron capture is much more probable. Hence, this mode of decay is frequently referred to as "K-capture." Orbital electron capture is also abbreviated as "EC."

K-capture is always accompanied by the emission of an x ray with energy equal to the difference between the K- and L-shell electron energy levels in the daughter product. Like positron emission, K-capture can be expected to occur in nuclides having a low n:p ratio. The intranuclear effect of either of these modes of decay is to change a proton into a neutron, thus increasing the n:p ratio.

c. Internal conversion is the process by which a nucleus in an excited energy state reaches a lower state by transferring its excess energy to an orbital electron (usually a K or L electron). The electron is ejected from the atom in lieu of a gamma ray of energy $h\nu$. The energy of the electron is $h\nu$ minus E_b, where E_b is the binding energy of the ejected electron.

d. Isomeric transition is a type of radioactivity associated with certain pairs of nuclides (called isomers) that have the same mass number and the same atomic number but exist in different nuclear energy states. Generally, one of the isomers is metastable (the nucleus is in an energy state above the ground state) and achieves the ground state or its lowest energy state by emitting delayed (usually greater than 10^{-9} seconds) gamma radiation. The metastable, or excited state, therefore represents one isomeric form of a particular nuclear species while the ground state represents the other. Further radioactive decay by beta or positron emission may proceed from the ground state.

e. Neutrinos are neutral particles with negligible rest mass. They account for the energy distribution among beta particles and positrons in these decay processes. On each beta or positron disintegration, the neutrino carries away some fraction of the disintegration energy. The neutrino is of no significance in nuclear medicine applications, because it seldom interacts with matter.

B. Transmutation

When a radioactive nuclide decays by α, β^-, β^+ or K-capture, a transmutation occurs. The decay product, or, as it is frequently called, the "daughter product," has become an atom of a new element with chemical properties entirely unlike the original "parent" atom.

A nucleus emitting an alpha particle disintegrates to a daughter element, reduced in atomic number by 2 and reduced in mass number by 4; e.g., radium decays by alpha emission to produce radon as follows:

$$^{226}_{88}\mathrm{Ra} \rightarrow {}^{222}_{86}\mathrm{Rn} + {}^{4}_{2}\mathrm{He}$$

In the case of beta emitters, the nucleus of the parent gives off a negatively charged particle resulting in a daughter more positive by one unit of charge; the atomic number increases by one but the mass number is unchanged; e.g., iodine-131 decays by beta emission to xenon-131 as follows:

$$^{131}_{53}\mathrm{I} \rightarrow {}^{131}_{54}\mathrm{Xe} + {}^{0}_{-1}\mathrm{e}$$

With positron emitters, the parent nucleus gives up a positive charge resulting in a daughter less positive by one unit of charge; the atomic number decreases by one and the mass number remains unchanged, as in the following example:

$$^{68}_{31}\mathrm{Ga} \rightarrow {}^{68}_{30}\mathrm{Zn} + {}^{0}_{1}\mathrm{e}$$

In instances where K-capture is the mode of decay, the transmutation is identical to that of positron emission:

$$^{125}_{53}\mathrm{I} + {}^{0}_{1}\mathrm{e} \rightarrow {}^{125}_{52}\mathrm{Te} + \text{x ray}$$

Nuclear decay reactions resulting in a transmutation often leave the resultant nucleus in an excited state. Nuclei, thus excited, may reach the ground state by the instantaneous emission of a gamma photon. The transmutation examples shown above are all accompanied by gamma emission on at least part of the disintegrations. There are numerous radionuclides, however, which decay by particulate emission alone.

C. Decay Phenomena

Each radioactive nuclide, artifical as well as natural, has its own unique characteristic pattern of decay. There are two aspects associated with this "pattern"; one being the types and energies of the emissions involved, and the other being the rate of decay.

All nuclei of a given nuclide seeking stability by radioactive decay do so in a specific manner. As previously indicated, $^{226}\mathrm{Ra}$ decays by alpha emission which is accompanied by a gamma photon. This represents the only mode of decay open to $^{226}\mathrm{Ra}$. There are, however, some radioactive nuclides which may decay with a branching effect whereby a choice of decay schemes exists. In such cases, a branching ratio is said to exist. A case in point is the decay of ^{57}Ni. This isotope of nickel decays 50% of the time by K-capture and 50% of the time by β^+ emission. The branching ratio is then

$$\frac{\beta^+}{EC} = 1$$

Not only do specific radionuclides disintegrate in a given manner insofar as the types of emissions are concerned, but the emissions from each nuclide exhibit a distinct energy picture. The energies associated with radiations are described in terms of "mega electron volts" (MeV) or "kiloelectron volts" (keV). Beta emissions may occur with energies up to about 5 MeV; alphas up to about 10 MeV; gamma photons up to approximately 3 MeV. The kinetic energy of a particle is proportional to the square of its velocity; or stated in reverse, the higher the energy the greater the velocity of the particle; whereas the velocity of photons is constant in a given medium and energy differences are manifested by varying wavelengths and frequencies.

The other characteristic aspect associated with decay patterns is the rate of decay. The disintegrations associated with radioactive nuclides occur with a regularity characteristic for each particular species. Such disintegrations are spontaneous and random, a single radium nucleus, for instance, may disintegrate at once or wait for thousands of years before emitting an alpha particle. All that can be predicted with any degree of certainty is that half of all the radium-226 nuclei present will disintegrate in 1622 years. This is called the half-life of ^{226}Ra.

The wide range in half-life values for naturally occurring radioactive elements is typified by ^{212}Po, with a half-life of 3×10^{-7} seconds, and ^{209}Bi, with a half-life of over 2×10^{18} years. The concept of half-life will be elaborated on more fully in Chapter III.

D. Radioactive Families

The tansmutations associated with natural radioactive elements frequently yield a daughter which also is radioactive. To date, there have been about 70 different natural radionuclides identified, each with its own characteristic pattern of radioactivity. Most of these yield radioactive daughters and are now known to be intimately interrelated in what are called radioactive series or families. It has been established that most of the isolated radioactive species belong to one of three independent groups or families. Each family starts with a parent radioelement decaying or transmuting into a daughter element, also radioactive, and so on until stability is attained. One family starts with uranium-238 and is called the urnaium series. Another starts thorium-232 and is called the thorium series, and a third starting with uranium-235 is called the actinium series. In each of these three series, there is a "seesawing" in the transmutation chain between decreasing the atomic number by two with α emission and increasing it by one with β^- emission. Each of these series ends in a different stable isotope of lead. There is also a fourth series, namely the neptunium series, named after its longest lived member. Actually, the neptunium series has been artificially produced and does not occur in nature, but it is assumed that it did occur in nature at one time and has become extinct because of the relatively short half-lives involved. The longest lived radioelement in the series is $^{237}_{93}$Np with a half-life of 2.2 x 10^6 years. Assuming that the age of the earth is 2.2 x 10^9 years, this would indicate that from the time of formation, neptunium-237 has undergone 1000 half-lives decay. The fraction of a radioelement remaining after 1000 half-lives would be fantastically small--of the order of 10^{-300}. It is obvious therefore, why it would be difficult to find traces of neptunium and its descendants in nature.

E. Singly Occurring Radioelements

Careful measurements have shown that almost all materials contain traces of radioactivity. One might suspect that these trace quantities of activity might be due to contamination with some of the heavy radioelements belonging to one of the radioactive series heretofore described. However, it is found that certain of the lighter elements are themselves weakly radioactive. The table below lists four examples of naturally occurring radioelements and their radiations.

Naturally Occurring Radionuclides

Nuclide	Half-Life	Emission Energies in MeV		
		Alpha	Beta	Gamma
$^{40}_{19}$K	1.26 x 10^9 y	---	1.314	1.460
$^{87}_{37}$Rb	5.0 x 10^{10}y	---	0.274	---
$^{147}_{62}$Sm	1.05 x 10^{11}y	2.23	---	---
$^{176}_{71}$Lu	3.0 x 10^{10}y	---	0.43	.088 .202 .306

Currently, there is no evidence that any series relationship exists among these nuclides. They, therefore, are regarded as individual, naturally occurring radionuclides having no familial relationships.

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CHAPTER III

UNITS OF RADIOACTIVE DECAY AND THE DECAY LAW

I. INTRODUCTION

The nuclear medical technologist frequently needs to calculate the activity of a radioactive material which was standardized at some previous time. Methods of performing these calculations and definitions of units of radioactive decay are included in the material which follows.

II. THE CURIE

Originally, the curie was based upon the disintegrations per second occurring in the quantity of radon gas in equilibrium with one gram of radium. If permitted to attain this equilibrium, one gram of radium will produce about 0.66 mm^3 of radon, and in this quantity of radon about 37 billion atoms disintegrate each second. Thus, originally the curie unit applied only to radium.

The International Radium Standard Commission in 1930 extended the definition to include that quantity of any radioactive decay product of radium that underwent the same number of disintegrations per second as one gram of radium. The Commission avoided specifying the precise amount, so for some years the exact value of the curie unit varied with each successive refinement in the measurement of the atomic weight of radium, which resulted in a more exact and stable value for the decay constant.

In 1950, the International Joint Commission of Standards, Units, and Constants of Radioactivity redefined the curie unit by accepting 37 billion disintegrations per second as amounting to a curie of radioactivity regardless of its source or characteristics. At present, the curie (Ci) is defined simply as a unit of activity equal to a disintegration rate of 3.7×10^{10} disintegrations per second. This definition of the curie is independent of the quantity of the radionuclide. Smaller and often more convenient units are the millicurie--one thousandth of a curie (mCi), and the microcurie--one millionth of a curie (μCi). The picocurie (3.7×10^{-2} dis/sec or 2.22 dis/min) is often used in expressing very low natural and environmental levels of radioactivity.

III. CURIES AND GRAMS: SPECIFIC ACTIVITY

Although the curie originally applied to emanations from one gram of radium, and one gram of radium is approximately one curie, it is important to note that the present definition of the curie does not make apparent what weight of the material is required. Since a curie of activity merely implies 37 billion disintegrations per second, the weight of the material required to produce this number of disintegrations per second will be a function of the decay rate of the atoms of the material (i.e., the disintegration constant) and of the number of atoms per gram of material. As examples, a curie of pure ^{60}Co would weigh less than 0.9 milligram, whereas a curie of natural ^{238}U would weigh over two metric tons. "Curies per gram" is termed "specific activity."

In nuclear medicine the term specific activity refers to the curies per gram of the compound and not the radionuclide alone. For example, one computes the specific activity of any pure radionuclide as follows:

$$\text{curies/gram} = \frac{1}{3.7 \times 10^{10}} \frac{N_A \lambda}{A}$$

where: N_A = Avogadro's number $\left(6.025 \times 10^{23} \frac{\text{atoms}}{\text{mole}}\right)$

A = atomic mass (gm/mole)

λ = decay constant (sec^{-1})

The constant 3.7×10^{10} is the number of disintegrations occurring per second in one curie of activity. For ^{131}I:

$$\text{specific activity} = \frac{(6.025 \times 10^{23})(10^{-6})}{(3.7 \times 10^{10})(131)} \text{curies/gm}$$

$$= 1.24 \times 10^{5} \text{ curies/gm}$$

When ^{131}I is combined with other atoms to form a compound, the molecular mass of the compound is substituted for the atomic mass to compute specific activity. For example, if iodine and sodium combine to make NaI, and assuming that every iodine atom in the compound is ^{131}I, the molecular mass becomes:

$$A = 23 + 131 = 154 \text{ gm/mole}$$

Likewise, Avogadro's number would have to have units of molecules/mole. Since N_A and λ have the same values as before, the specific activity of the compound is less than that of the radionuclide by the factor 131 ÷ 153.

Or, $\text{specific activity} = (1.24 \times 10^{5})(131/154)$

$$= 1.06 \times 10^{5} \text{ curies/gm}$$

If the "tag" is not perfect the specific activity may be further reduced. For example, if only one half the iodine atoms in the NaI molecules are ^{131}I, the specific activity would be reduced by a factor of 2, or,

$$\text{specific activity} = 5.3 \times 10^{4} \text{ curies/gm}$$

IV. THE RADIOACTIVE DECAY LAW

A. The Disintegration Constant

The activity of any sample of radioactive material decreases or decays at a fixed rate which is characteristic of that particular radionuclide. No known physical or chemical agents (such as temperature, pressure, dissolution, or combination) may be made to influence this rate. The rate may be characterized in at least two ways, one of which is the disintegration constant (λ). The disintegration constant represents the fraction of the total number of atoms present which decays in unit time. Thus the number of disintegrations occurring per unit time in a given sample is the product of the number of atoms present in the sample (N) and the fraction of these disintegrating in each unit of time (λ), or:

$$-\frac{dN}{dt} = \lambda N$$

where the minus sign is used to indicate that the number of atoms is diminishing. Integration of the above equation leads to the basic law of radioactive decay:

$$N_t = N_0 e^{-\lambda t}$$

Stated in words, the number of atoms (N_t) remaining after a time (t) is equal to the number (N_0) at time (t_0) multiplied by $e^{-\lambda t}$, where e is the base of the natural system of logarithms and λ is the disintegration constant.

B. The Half-Life

The disintegration constant is not so conveniently used as is another means of representing the rate of radioactive decay, viz., the half-life ($T_{\frac{1}{2}}$) of the radionuclide. The half-life is merely the length of time required for one half of the radioactive atoms present initially to disintegrate. The half-life can be shown to be related to the disintegration constant (λ) in the following way:

$$\lambda = \frac{0.693}{T_{\frac{1}{2}}}$$

Therefore, one may substitute this expression for (λ) in the basic decay law which yields:

$$N_t = N_0 e^{-\frac{0.693\, t}{T_{\frac{1}{2}}}}$$

If it is desired to write the equation in terms of activity (A) instead of numbers of atoms, one can multiply both sides of the equation by the disintegration constant (λ) as follows:

$$\lambda N_t = \lambda N_0 e^{-\frac{0.693\, t}{T_{\frac{1}{2}}}}$$

but, $\lambda N = A$

Therefore: $A_t = A_0 e^{-\frac{0.693\, t}{T_{\frac{1}{2}}}}$

This is the working equation for computing the activity of a radionuclide remaining in a sample after it has undergone decay for some time interval.

C. Calculation of Activity

Example:

Given: A_o = 10 mCi of ^{32}P

t = 120 days

$T_{\frac{1}{2}}$ = 14.2 days

Find A_t, the quantity remaining after 120 days.

1. Computational Method

$$A_t = (10)e^{-\frac{(0.693)(120)}{14.2}} \text{ mCi}$$

$$= 10\ e^{-5.85} = 10(0.00288) \text{ mCi}$$

$$A_t = 0.0288 \text{ mCi}$$

This is the type of calculation which would be required before diluting a radioisotope for future use, or for determining the activity remaining in a quantity of nuclide which had been stored for some time since its standardization.

2. Graphic Method

There is a graphical method of accomplishing this same result. It is based on the fact that each half-life reduces the activity by one half, and the effect is cumulative: i.e., two half-lives reduce the activity to $\frac{1}{2} \times \frac{1}{2}$ or $\frac{1}{4}$; three to $\frac{1}{2} \times \frac{1}{2} \times \frac{1}{2}$ or $\frac{1}{8}$, etc. In the general case,

$$A_n = A_o\left(\tfrac{1}{2}\right)^n$$

where (n) is the number of half-lives elapsed. On pages 24 and 25, this function is graphed. The answer to the example problem may be read from the graph at the point where the line intersects 8.44, the number of half-lives ^{32}P undergoes in 120 days. A useful rule of thumb is that seven half-lives will reduce any activity to below 1% of its original value.

V. SERIES DECAY[1]

Series decay concerns the mathematical relationships between two or more radionuclides existing in a decay chain. An example of a decay chain is the two step decay of the fission product, ^{90}Sr:

$$^{90}Sr \xrightarrow{\beta^-} {}^{90}Y \xrightarrow{\beta^-} {}^{90}Zr \quad \text{(stable)}$$

---

[1] The student who has not studied integral calculus may wish to skip the remainder of this chapter.

The solution for three or more nuclides, although straight forward, is quite involved. A two-step relationship (parent-daughter) can be readily derived and is reasonably easy to apply. Parent-daughter relationships are presently being exploited as sources of radioisotopes for use in nuclear medicine.

A. General Relationships

Decay of the parent nuclide is described by the equation:

$$\frac{dN_1}{dt} = -N_1\lambda_1$$

or

$$dN_1 = -N_1\lambda_1\,dt$$

For the daughter nuclide, assuming a freshly purified sample of parent material:

$$\frac{dN_2}{dt} = N_1\lambda_1 - N_2\lambda_2$$

where the $N_1\lambda_1$ represents the rate at which atoms of the daughter are formed, and the $N_2\lambda_2$ term represents their rate of disappearance.

Upon integration,

$$N_2 = \frac{\lambda_1}{\lambda_2-\lambda_1} N_1^o \left(e^{-\lambda_1 t} - e^{-\lambda_2 t}\right) + N_2^o e^{-\lambda_2 t}$$

where:

N_1^o = initial number of parent atoms present

N_2^o = initial number of daughter atoms present

N_2 = number of daughter atoms at time t

λ_1 = decay constant of parent

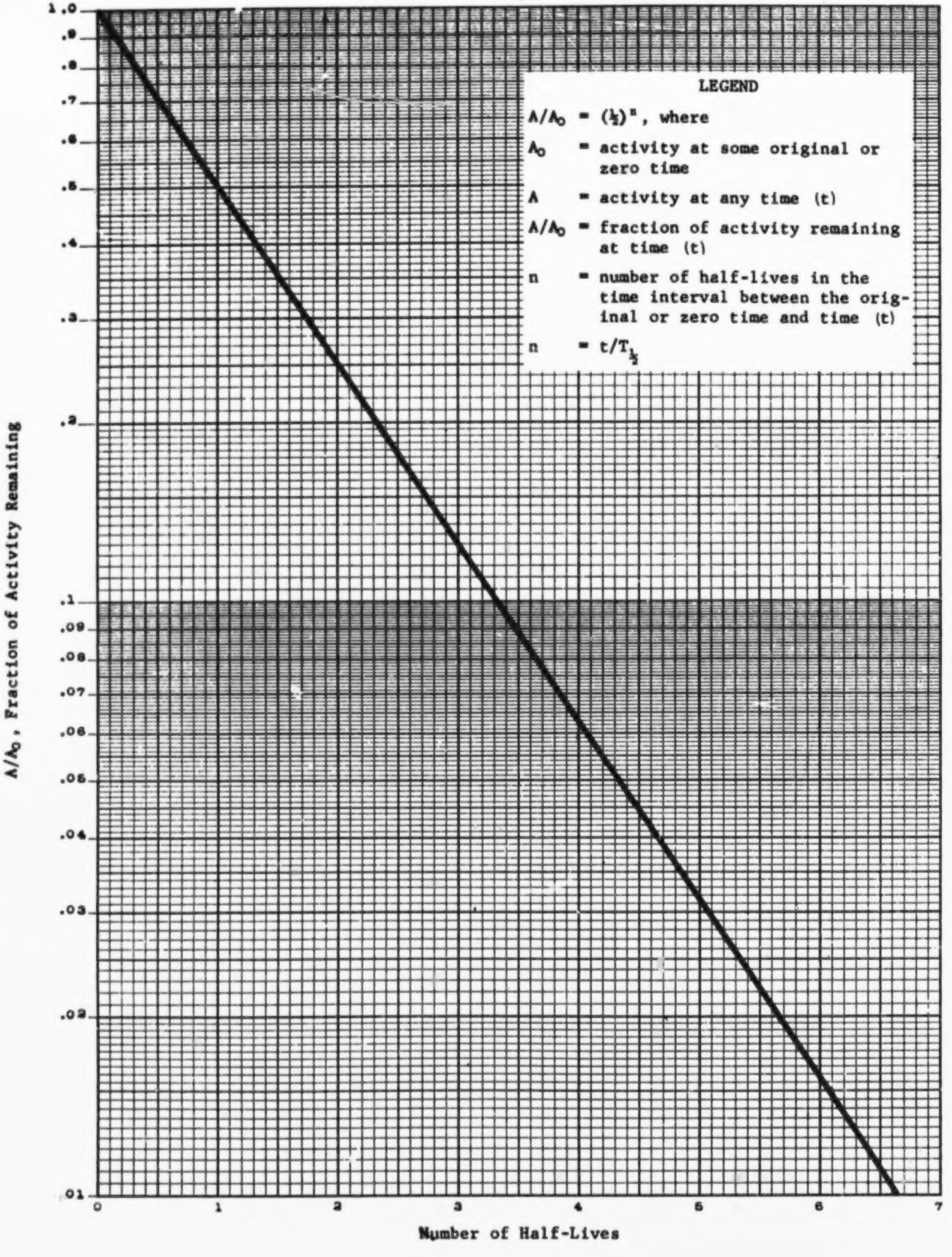
λ_2 = decay constant of daughter

t = time elapsed since initial observation.

The equation for N_2 can be converted to units of activity by multiplying both sides of the equation by λ_2.

$$A_2 = \frac{\lambda_2}{\lambda_2-\lambda_1} A_1^o \left(e^{-\lambda_1 t} - e^{-\lambda_2 t}\right) + A_2^o e^{-\lambda_2 t}$$

This equation is the most general form and can be used for any parent-daughter relationship. However, the equation may be simplified if certain relationships between λ_1 and λ_2 exist.



Radioactive Decay, Semi-Log Plot

LEGEND

A/A_0 = $(\frac{1}{2})^n$, where

A_0 = activity at some original or zero time

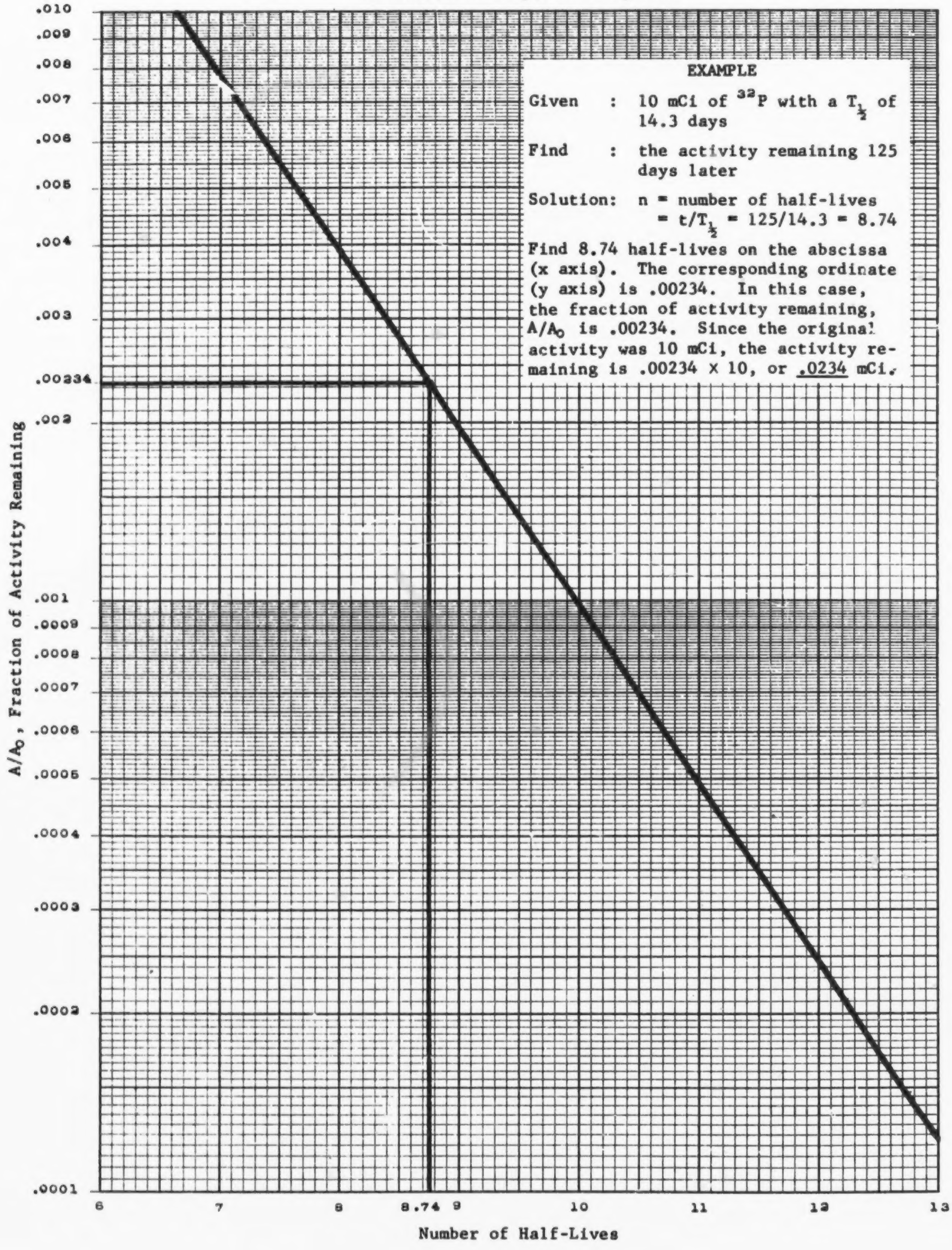
A = activity at any time (t)

A/A_0 = fraction of activity remaining at time (t)

n = number of half-lives in the time interval between the original or zero time and time (t)

n = $t/T_{\frac{1}{2}}$

Radioactive Decay, Semi-Log Plot



EXAMPLE

Given : 10 mCi of ^{32}P with a $T_{\frac{1}{2}}$ of 14.3 days

Find : the activity remaining 125 days later

Solution: n = number of half-lives = $t/T_{\frac{1}{2}}$ = 125/14.3 = 8.74

Find 8.74 half-lives on the abscissa (x axis). The corresponding ordinate (y axis) is .00234. In this case, the fraction of activity remaining, A/A_0 is .00234. Since the original activity was 10 mCi, the activity remaining is .00234 × 10, or .0234 mCi.

B. Special Cases

1. Secular Equilibrium: $\lambda_2 >> \lambda_1$

In secular equilibrium, the half-life of the parent is much longer than the half-life of the daughter. In fact, the parent half-life may be considered as infinite compared to the time of observation. Buildup of activity in a freshly isolated parent fraction occurs as shown in Figure III-1.

For the period up to equilibrium (about 7 daughter half-lives), the general equation reduces to:

$$A_2 = A_1^0 \left(1 - e^{-\lambda_2 t}\right).$$

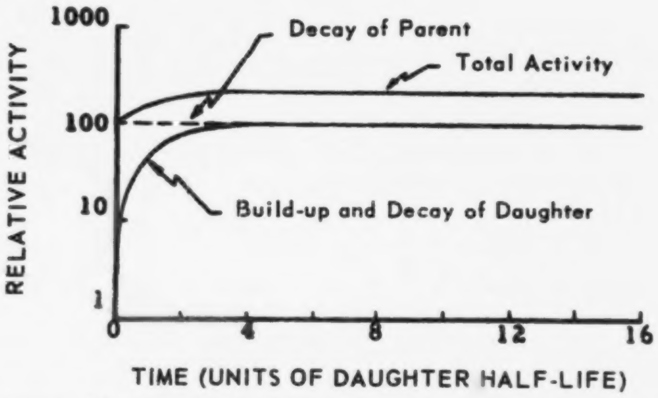


Figure III-1.--Parent Daughter Relationship in Secular Equilibrium

At secular equilibrium $A_2 = A_1$, i.e., the activity of the daughter is equal to the activity of the parent. After significant decay of the parent the following equation applies:

$$A_2 = A_1^0 \, e^{-\lambda_1 t}$$

An example of secular equilibrium is the decay of $^{90}Sr + ^{90}Y$.

2. Transient Equilibrium: $\lambda_2 > \lambda_1$

In transient equilibrium, the half-life of the parent is longer than that of the daughter, but cannot be considered infinite. In a freshly purified parent fraction, the daughter activity builds up, then decays with the same half-life as the parent. This relationship is illustrated in Figure III-2.

At equilibrium:

$$A_2 = \frac{\lambda_2}{\lambda_2 - \lambda_1} A_1$$

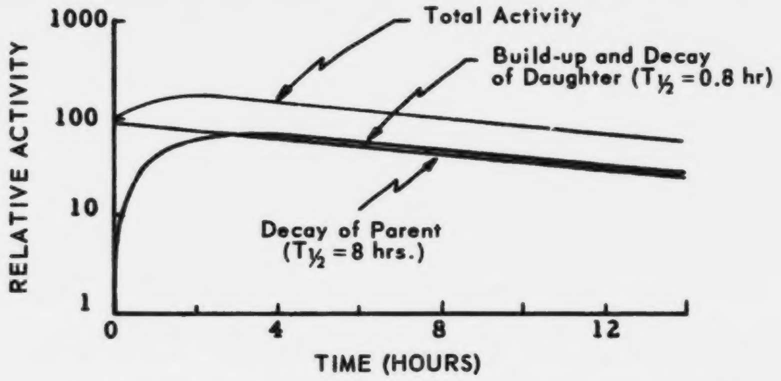


Figure III-2.--Parent-Daughter Relationship
in Transient Equilibrium

Note that the daughter activity is greater than that of the parent by the factor

$$\frac{\lambda_2}{\lambda_2 - \lambda_1}$$

An example of transient equilibrium is the decay of ^{99}Mo to ^{99m}Tc.

3. No Equilibrium: $\lambda_1 > \lambda_2$

Here the half-life of the parent is shorter than that of the daughter and no equilibrium condition is reached. The relationship of the parent and daughter, in this case, is as shown in Figure III-3.

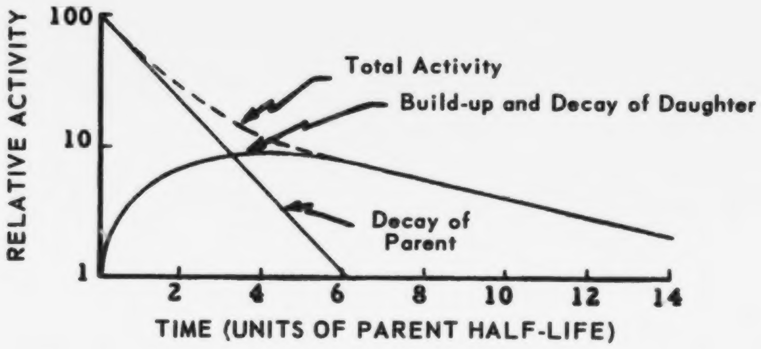


Figure III-3.--Parent-Daughter Relationship
Where No Equilibrium Exists

VI. SUMMARY

The most widely used unit to express a quantity of radioactive material is the curie or some submultiple of the curie. Radioactive decay may be calculated or graphically determined if the half-life of the material of interest is known. Parent-daughter relationships are rather complicated to compute, but may be simplified by taking advantage of equilibrium conditions which may exist.

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CHAPTER IV

NUCLEAR REACTIONS

I. INTRODUCTION

A nuclide may be changed into another nuclide (a phenomenon known as transmutation) by bombarding it with charged particles, neutrons or photons. This process is important, since the product nucleus of the reaction may be radioactive and the secondary particles given off may cause other reactions. Many radionuclides used in nuclear medicine are produced by this mechanism.

II. NUCLEAR REACTIONS WITH CHARGED PARTICLES AND PHOTONS

A. Components of the Reaction

The initial, intermediate, and final steps of a typical nuclear reaction involve five components, as shown below:

$$\begin{bmatrix}\text{Target}\\ \text{Nucleus}\end{bmatrix} + \begin{bmatrix}\text{Bombarding}\\ \text{Particle}\end{bmatrix} \longrightarrow \begin{bmatrix}\text{Compound}\\ \text{Nucleus}\end{bmatrix} \longrightarrow \begin{bmatrix}\text{Product}\\ \text{Nucleus}\end{bmatrix} + \begin{bmatrix}\text{Product}\\ \text{Particle}\end{bmatrix}$$

Examples of a bombarding particle or projectile are an alpha or beta particle, a gamma photon, a proton, or a deuteron. Sources of these may be fission, fusion, radioactive decay, or particle accelerators.

The target nucleus may be any nucleus ranging from that of the lightest atom, hydrogen, to one of the heaviest, e.g., uranium.

The product nucleus is the nuclear species formed as a result of the breakdown of the compound nucleus.

The product particle may be any of the subatomic particles. More than one product particle may be released.

The compound nucleus, containing the target nucleus plus the bombarding particle, exists for only 10^{-12} seconds or less. During this lifetime, the excess energy of the particle is distributed throughout the nucleus and the incident particle loses its identity. The method of breakdown of the compound nucleus is dependent only on the excess energy contained, and not on the method of formation. Disintegration of the compound nucleus differs from radioactive decay in two ways: (1) The lifetime of the compound nucleus is always extremely short; and (2) protons are not converted into neutrons and neutrons are not converted into protons during the process of change.

B. Compound Nucleus Formation

The extent of nuclear interaction depends on the nature of the projectile, its energy, and the material being bombarded.

Positively charged particles must overcome a potential energy barrier due to electrostatic forces of repulsion before they can react with a nucleus. This repulsive force is proportional to the charge on both the target and projectile, and the greater the charge, the greater the energy necessary to overcome the barrier. For this reason, reactions occur most easily between projectile particles and targets of low atomic number.

Beta particles and photons interact primarily with electrons and are thus more effective in bomarding a nucleus having few orbital electrons, i.e., of low atomic number. Since these projectiles can offer little or no mass energy to the compound nucleus, they must have kinetic energy greater than the binding energy of a nucleon (proton or neutron) before a particle can be ejected from the target nucleus. For this reason, transmutation by beta particles and photons of energies less than 5 MeV will occur only in special cases. At high energies, these projectiles can cause many transmutations.

C. Conditions for Decay

Three laws may be applied to most nuclear reactions involving energy changes of less than a few MeV: (1) conservation of mass number, (2) conservation of atomic number, and (3) conservation of energy. These laws simplify the writing of reactions and the prediction of possible products.

For the mass number to be conserved, the total number of nucleons included in the system before the reaction must equal the total number after the reaction.

For the atomic number to be conserved, the number of protons in the system must remain constant. Thus, no protons can be changed into neutrons (as in electron capture) nor can any neutrons be changed into protons (as in beta decay). The total number of neutrons also remains constant.

Conservation of energy specifies that the total energy on one side of the equation must equal that on the other. Since in a nuclear reaction, mass may be converted into energy, the factor being conserved is designated as:

$$\begin{bmatrix}\text{Kinetic}\\\text{Energy}\end{bmatrix} + \begin{bmatrix}\text{Mass}\\\text{Energy}\end{bmatrix}$$

where the equivalence of mass and energy is computed by the relationship:

$$1 \text{ atomic mass unit} = 931 \text{ MeV}$$

The following is an example of the application of the principle of conservation of total energy:

$${}^{14}_{7}\mathrm{N} + {}^{4}_{2}\mathrm{He} \longrightarrow \left[{}^{18}_{9}\mathrm{F}\right] \longrightarrow {}^{17}_{8}\mathrm{O} + {}^{1}_{1}\mathrm{H}$$

$$14.003074 + 4.002603 \longrightarrow 16.999133 + 1.007825$$

$$\Delta m = \text{Mass}_{\text{products}} - \text{Mass}_{\text{reactants}}$$

$$\Delta m = 18.006958 - 18.005697 = +0.001261$$

$$\Delta E = 931 \frac{\text{MeV}}{\text{amu}} (0.001261)\,\text{amu} = 1.17\ \text{MeV}$$

Since there is a gain in mass, 1.17 MeV of excess energy must be supplied to produce this reaction. If atomic weights of the target and product nuclei are used, such calculations will be accurate only if atomic weights are also used for the bombarding and product particles. In this way, the total mass of the electrons on each side of the equation balances out.

III. EXPRESSING NUCLEAR REACTIONS

Several shorthand methods can be used to indicate nuclear reactions.

The reaction,

$$^{23}_{11}\text{Na} + {}^{1}_{1}\text{H} \longrightarrow \left[^{24}_{12}\text{Mg}\right] \longrightarrow {}^{23}_{12}\text{Mg} + {}^{1}_{0}\text{n}$$

can also be written:

$$^{23}\text{Na}\ (\text{p,n})\,^{23}\text{Mg}.$$

Since only three of the four products and reactants of a reaction are necessary to balance the equation, this reaction could also be designated by: $^{23}\text{Na}\ (\text{p,n})$.

IV. TYPICAL REACTIONS

Depending on the energy of the bombarding particle and its probability of interaction with a target nucleus, nuclear reactions can be classified in a number of ways. These reactions are general and cannot be assumed to occur with any particular target nucleus.

A. Proton-Induced

The (p,γ) and (p,n) reactions are common with targets of low atomic number. A typical example is:

$$^{27}_{13}\text{Al} + {}^{1}_{1}\text{H} \longrightarrow {}^{28}_{14}\text{Si} + \gamma$$

High-energy protons can cause (p,2n) and (p,pn) reactions. Three or four particles may be emitted if the proton energy is several hundred MeV.

B. Deuteron-Induced

The most common deuteron-induced reactions are the (d,p) and (d,n) reactions:

$$^{130}_{52}\text{Te} + {}^{2}_{1}\text{H} \longrightarrow {}^{131}_{53}\text{I} + {}^{1}_{0}\text{n}$$

At high energies, (d,2n) or (d,α) reactions may also occur.

C. Alpha-Induced

A number of reactions of the (α,n) type may occur if the target nucleus is an element of fairly low atomic number. The reaction,

$$^{9}_{4}Be + ^{4}_{2}He \longrightarrow ^{12}_{6}C + ^{1}_{0}n,$$

led to the discovery of the neutron by Chadwick in 1932. This reaction is now a common laboratory source of neutrons, the alpha particles being supplied by a radionuclide such as polonium or plutomium. Multiple particle emissions, such as (α,2n), (α,3n), and (α,np), will occur when alpha particles of very high energy are used as projectiles.

D. Electron-Induced (beta particle)

An example of a reaction of this type is:

$$^{9}_{4}Be + ^{0}_{-1}e \longrightarrow ^{8}_{4}Be + ^{1}_{0}n + ^{0}_{-1}e.$$

It is interesting to note that the electron simply provides energy for the reaction while passing through or very near the target nucleus. A number of nuclear transmutations (or excitations) are possible with high-energy electrons.

E. Photon-Induced

The following are two examples of (γ,n) reactions, often called "photodisintegration":

$$^{2}_{1}H + \gamma \longrightarrow ^{1}_{1}H + ^{1}_{0}n$$

and

$$^{9}_{4}Be + \gamma \longrightarrow ^{8}_{4}Be + ^{1}_{0}n.$$

The first reaction was used to compute the mass of the neutron by Goldhaber and Chadwick in 1934. Many additional transmutations by photons are possible at higher energies (greater than 20 MeV).

F. Neutron-Induced

Before discussing neutron reactions, it is necessary to review neutron properties.

1. Properties of neutrons

The neutron has a mass number of 1, an atomic number (nuclear charge) of 0, and an atomic mass of 1.008665 amu. Because it has no electrical charge the neutron can penetrate relatively easily into a nucleus.

Free neutrons are unstable (radioactive) and disintegrate by beta emission with a half-life of approximately 13 minutes. The resultant decay product is a proton.

Neutron radiations are classified on the basis of their kinetic energies. The most probable velocity of free neutrons in various substances at ordinary room temperature is approximately 2200 meters per second. Their kinetic energy may be calculated from the equation:

$$E = \tfrac{1}{2} mv^2$$

where: m = neutron mass in grams

v = neutron velocity in cm/sec.

Substituting:

$$E = \tfrac{1}{2}\,(1.66 \times 10^{-24}\ \text{gm})(2.2 \times 10^5\ \text{cm/sec})^2$$

$$= 4.0 \times 10^{-14}\ \text{ergs}$$

$$= 0.025\ \text{eV}.$$

Neutrons with this average kinetic energy at 20° are called thermal neutrons. Epithermal, or slow neutrons range in energy from 0.025 eV to 100 eV. Intermediate neutrons range in energy from 100 eV to 10^5 eV. Fast neutrons possess energies from 10^5 eV to 20 MeV. Relativistic neutrons have energies in excess of 20 MeV.

Classification of neutrons according to kinetic energy is important from two standpoints: (a) the interaction of neutrons with the nuclei of atoms differs with the neutron energy, and (b) the methods of producing, detecting and shielding against the various classes of neutrons are different.

Detection of neutrons is relatively difficult, due to the lack of ionization along their paths; negligible response to externally applied electric, magnetic or gravitational fields; and the fact that they interact only with atomic nuclei, which are exceedingly small.

2. Neutron reactions

Radiative capture with gamma emission is the most common type of reaction for slow (thermal) neutrons. This (n,γ) reaction often results in product nuclei which are radioactive. For example:

$$^{59}_{27}\text{Co} + {}^{1}_{0}\text{n} \longrightarrow {}^{60}_{27}\text{Co} + \gamma.$$

This process of converting a stable nucleus to its radioactive counterpart by neutron bombardment is called "neutron activation." Many radionuclides used in nuclear medicine are produced by this process.

A second type of general reaction is that giving rise to a charged particle. Typical examples include (n,p), (n,d), and (n,α) reactions, i.e., reactions in which a proton, a deuteron, or an alpha particle is ejected from the target nucleus.

A third type of neutron-induced nuclear reaction is fission. Fission occurs following the absorption of a neutron by several of the very heavy elements. When ^{235}U nuclei undergo fission by neutrons, an average of 2 to 3 neutrons are expelled from each nucleus along with associated gamma radiation. Each nucleus splits into two smaller nuclei which are called primary fission products or fission fragments, and these products usually undergo radioactive decay to form secondary fission product nuclei. As an example, if one neutron fissions a ^{235}U nucleus, it could yield yttrium-95, iodine-139, two neutrons, and fission energy. There are some 30 different ways that fission may take place with the production of about 60 primary fission fragments. These fragments and the atoms which result from their decay are referred to as fission products, and they number between 400 and 600, according to the type and number of nucleons their nuclei possess.

Many fission products have found application in medicine, industry, and research. A well known example is ^{131}I which is used extensively in medicine as both a diagnostic and therapeutic agent.

The fission process is the source of energy for nuclear reactions and some types of nuclear weapons. Also, neutrons generated from the fissioning of the fuel in a reactor are used to activate stable materials to a radioactive form as previously discussed. Many radioisotopes used in medicine are produced in this manner.

Neutron scattering may be listed as a fourth type of general reaction. Scattering of neutrons by elastic or inelastic collision is the principal mechanism of moderation or slowing down of fast neutrons to thermal energies. Scattering of neutrons is not of general interest in nuclear medicine and will not be discussed here in detail.

3. Reactions in biological systems

Fast neutrons lose energy in soft tissue, mainly by repeated scatterings with hydrogen nuclei. The hydrogen nuclei are themselves scattered in the process and become recoil protons which cause ionization.

Slow neutrons are captured in soft tissue and release energy by two principal mechanisms:

$$^{1}_{0}n + {}^{1}_{1}H \longrightarrow {}^{2}_{1}H + \gamma \text{ (2.2 MeV)}$$

and

$$^{1}_{0}n + {}^{14}_{7}N \longrightarrow {}^{14}_{6}C + {}^{1}_{1}H \text{ (0.66 MeV)}$$

The gamma and proton energies may be absorbed in the tissue and cause cellular damage.

V. SUMMARY

Whenever charged particles, neutrons and photons, are able to penetrate the nucleus, transmutations may be caused which often result in artificial radioactivity. The bombarding projectile can be a neutron, proton, deuteron, alpha particle, electron, or gamma photon. Such bombarding particles may originate from other transmutations, radioactive decay, fission, fusion, or particle accelerators. As a result of the interaction of the projectile and target, a compound nucleus is formed, exists for an instant, and then separates into a product particle and product nucleus. Three laws govern these reactions: (1) conservation of mass number; (2) conservation of atomic number; and (3) conservation of total energy.

SUGGESTIONS FOR FURTHER READING

1. Lapp, R. E., and Andrews, H. L., Nuclear Radiation Physics, Prentice-Hall, Inc. (1964), chap. 11.

CHAPTER V

INTERACTION OF RADIATION WITH MATTER

I. INTRODUCTION

All radiation possesses energy either inherently, as in the case of electromagnetic radiation, or kinetic energy of motion as in the case of the particulate radiations. Absorption of radiation is the process of transferring this energy to the atoms of the medium through which the radiation is passing. To say that radiation interacts with matter is to say that it is either scattered or absorbed. The mechanisms of absorbing radiation are of fundamental interest in nuclear medicine because absorption is the principle upon which detection is based. The transfer of energy from the emitted particle or photon to atoms of the absorbing material may occur by several mechanisms, but of the radiations commonly encountered, the following two are the most improtant:

1. Ionization - any process that results in the removal of an electron (negative charge) from an atom or molecule thereby leaving the atom or molecule with a net positive charge.

2. Excitation - the addition of energy to an atomic or molecular system, thereby exciting it from its ground state to a higher energy state. Depending on the type of interaction, either the atomic nucleus or one of its orbital electrons may absorb the excitation energy.

Ordinarily, the atoms in a material are electrically neutral, i.e., they have exactly as many negative electrons in orbit as there are positive protons in the nucleus. Thus, the net electrical charge is zero. Radiations have the ability either to remove one or more of the electrons from their orbits or to raise the orbital electrons to a higher energy level. In ionization, an atom carrying an excess of positive charge and a free electron are left behind. In electronic excitation, the excited atom may lose its excess energy vacancy created in the excitation process. When this occurs, the excess energy is liberated as a photon of electromagnetic radiation which may undergo other absorptive processes. Nuclear excitation is of significance only for neutrons or other radiations of relatively high energies. A discussion of the types of radiations and their interactions might conveniently be divided into four main categories:

1. Heavy, positively charged particles: Alpha particles, protons, deuterons, and tritons exhibit similar mechanisms of interaction with matter. Alpha particles will be discussed as a prototype of this group.

2. Beta particles: Both positrons and electrons fall into this category. They have equal masses and equal but opposite charges, and therefore lose their kinetic energy by similar mechanisms. The electron is discussed as the prototype of this category.

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3. Electromagnetic radiation: This group includes both x and gamma radiation; however, since these two radiations differ only in their origin and not in the mechanisms of interaction, only gamma radiation will be discussed.

4. Neutrons: The interactions of neutrons were discussed in chapter IV, and will not be included in this chapter.

II. ALPHA ABSORPTION

An alpha particle is made up of two protons (positively charged) and two neutrons, all strongly bound together by nuclear forces. If such a particle approaches an electron (negatively charged), it experiences a strong electrostatic attraction, whereas if it approaches an atomic nucleus (positively charged), it will experience a repulsive force. Alpha particles have a mass about 8,000 times that of the electron. They are ejected from the nuclei of radioactive atoms with velocities of the order of 1/20 the speed of light. All of these properties -- its large mass, its charge, and its high velocity--make the alpha particle an efficient projectile when it encounters atoms of an absorbing material. In other words, it would have a high probability of interacting or colliding with orbital electrons and atomic nuclei.

When speaking of "collisions" between subatomic particles, it is understood that the particles need approach each other only sufficiently close for their force fields to interact. Such an interaction may then be referred to as a collision. Some collisions result in ionization and/or excitation. Since a finite amount of energy is required to ionize or excite an atom, the kinetic energy of the alpha particle is gradually dissipated by such interactions until it captures two electrons and settles down to a quiet existence as a helium atom.

Due to the high probability of interaction between an alpha particle and orbital electrons of the absorbing medium, a large number of ion pairs is formed per unit of path length of the alpha particle. And since a fraction of the kinetic energy of the alpha particle is lost in forming each ion pair, alpha particles lose their energy over a relatively short distance. For these reasons, the range of alpha particles is much less than the range of other types of ionizing radiation. A single sheet of paper is sufficient to absorb all alpha particles emitted from most radionuclides. The alpha particle is, in summary, a highly ionizing, weakly penetrating type of radiation.

III. BETA ABSORPTION

The rest mass of a beta particle is the same as that of an orbital electron and, hence is much less than the mass of the nuclei of the atoms making up the absorbing medium. Since beta particles and orbital electrons have like charges, they experience an electrostatic repulsion when in the vicinity of one another. But a beta particle has a charge opposite to that on the atomic nucleus, therefore an electrostatic attraction will be experienced as the beta approaches the nucleus.

These facts are important in understanding the interaction between the beta radiation and the atoms in an absorbing medium. For example, considering only the mass relationship between the beta particles and the orbital electrons, one might expect that the interaction between two electrons is somewhat similar to the collisions between billiard balls. Actually, a beta particle may lose all of its energy in a single collision with another electron. In such an interaction, the target electron can itself become an ionizing particle.

Normally, a beta particle loses its energy in a large number of ionization and excitation events in a manner analogous to the alpha particle. Due to the smaller size and charge of the electron, however, there is a lower probability of beta radiation interacting in a given thickness of material. Consequently, the range of a beta particle is considerably greater than that of an alpha particle of comparable energy.

Since the electron mass is small compared with the mass of a nucleus, large deflections can occur in single collisions, particularly when electrons of low energies are scattered by high atomic number elements (high positive charge on the nucleus). As a result, a beta particle may have an interaction with an atom which results in the production of x rays. A high energy beta particle may penetrate through the electron cloud surrounding the nucleus of an atom and experience the strong electrostatic force of the nucleus resulting in a change in velocity and the emission of an x ray. Such x rays are referred to as "bremsstrahlung radiation." It becomes an increasingly important mechanism of energy loss as the initial energy of the beta particle increases and the atomic number of the absorbing medium increases. As previously pointed out, most alpha particles from a given radionuclide are emitted with about the same energy. When betas are emitted, the total kinetic energy involved in the decay of the radioactive atom is divided between the beta particle and a neutrino. The neutrino has zero charge and negligible mass. It carries away a fraction of the total kinetic energy available in every beta disintegration. Therefore, the beta particles from a given radionuclide are emitted with a spectrum of energies varying from practically zero up to some maximum energy which is characteristic of the radionuclide.

IV. GAMMA INTERACTIONS

Because gamma radiation is of primary interest in nuclear medicine, gamma interactions are discussed here in more detail.

Since gamma photons have both an electric and a magnetic field component they interact electrically with atoms to produce ionization even though they possess no net electrical charge. There are twelve known processes by which gamma rays interact with matter. However, the three most important interactions are the photoelectric effect, the Compton effect, and pair production.

1. Photoelectric Effect

The photoelectric effect predominates when gamma rays of low energies interact with high atomic number absorbers. The gamma ray, or photon, imparts all of its energy to an orbital electron of an atom and the photon vanishes. Thus, the process may be considered as a complete energy loss process. In order for momentum to be conserved, another body must be present, so gamma photons can not interact with free electrons via the photoelectric effect. Most photoelectric interactions are with K shell or tightly bound electrons.

The gamma photon energy is imparted to the orbital electron in the form of kinetic energy of motion, and this greatly increased energy overcomes the attractive force of the nucleus for the electron and causes the electron to be ejected from its orbit with considerable velocity. (See Figure V-1.)

The kinetic energy of the ejected electron (called a photoelectron) is expressed as

$$KE = E_\gamma - W$$

where KE = kinetic energy of the photoelectron

E_γ = energy of the incident gamma photon

W = binding energy of the electron to the nucleus of the atom

For most photon energies of interest in nuclear medicine, W is small in relation to E_γ except for high atomic number absorbers.

When the photoelectron is ejected an ion pair results. The photoelectron may have sufficient energy to ionize other atoms thus producing secondary ion pairs until all of its energy is expended. After the photoelectron is ejected, the vacancy in the electron shell is filled with another electron from an outer shell. The excess energy is emitted in the form of one or more characteristic x rays or an ejected outer orbital electron, known as an Auger electron.

2. Compton Effect

The Compton effect is the dominant interaction when intermediate energy gammas interact in low atomic number absorber material. The Compton effect results in the transfer of only part of the energy of the incoming gamma ray to the absorbing medium. The effect may be considered as an inelastic, incoherent scattering of the rays by atomic electrons. Again the gamma ray interacts with an orbital electron, but in the case of Compton interactions, only a part of the energy is transferred to the electron, and another gamma ray of lower energy than the primary one is emitted. (See Figure V-2.)

The high velocity electron, now referred to as a Compton electron, produces secondary ionization in the same manner as does the photoelectron, and the weakened gamma ray, called a scattered photon, continues on until it loses more energy in another Compton interaction or disappears completely via the photoelectric effect. A gamma photon may undergo several scattering events before it is finally absorbed.

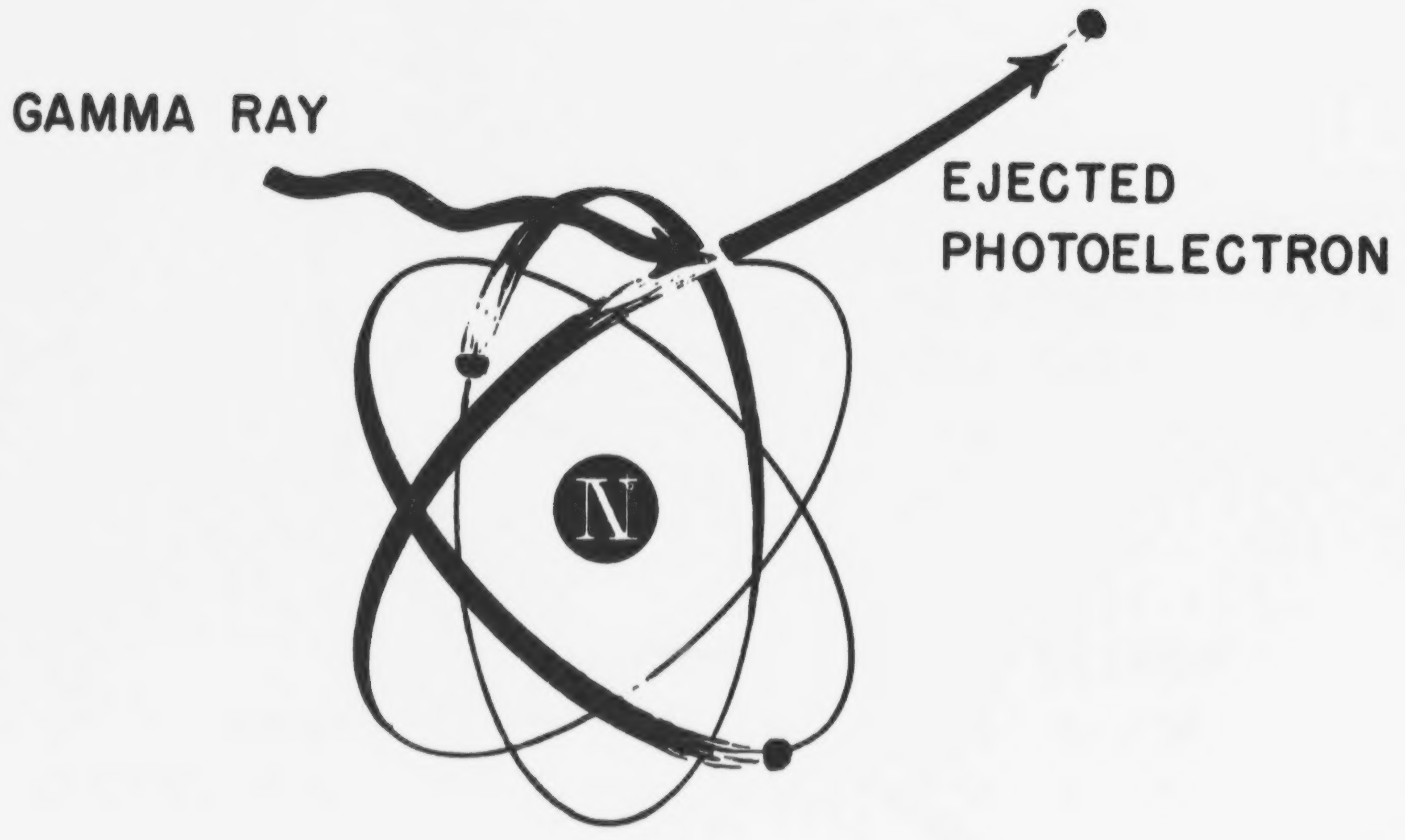
GAMMA RAY
EJECTED PHOTOELECTRON
N

Figure V-1.--Photoelectric Effect
(Primarily Low-Energy Photons)

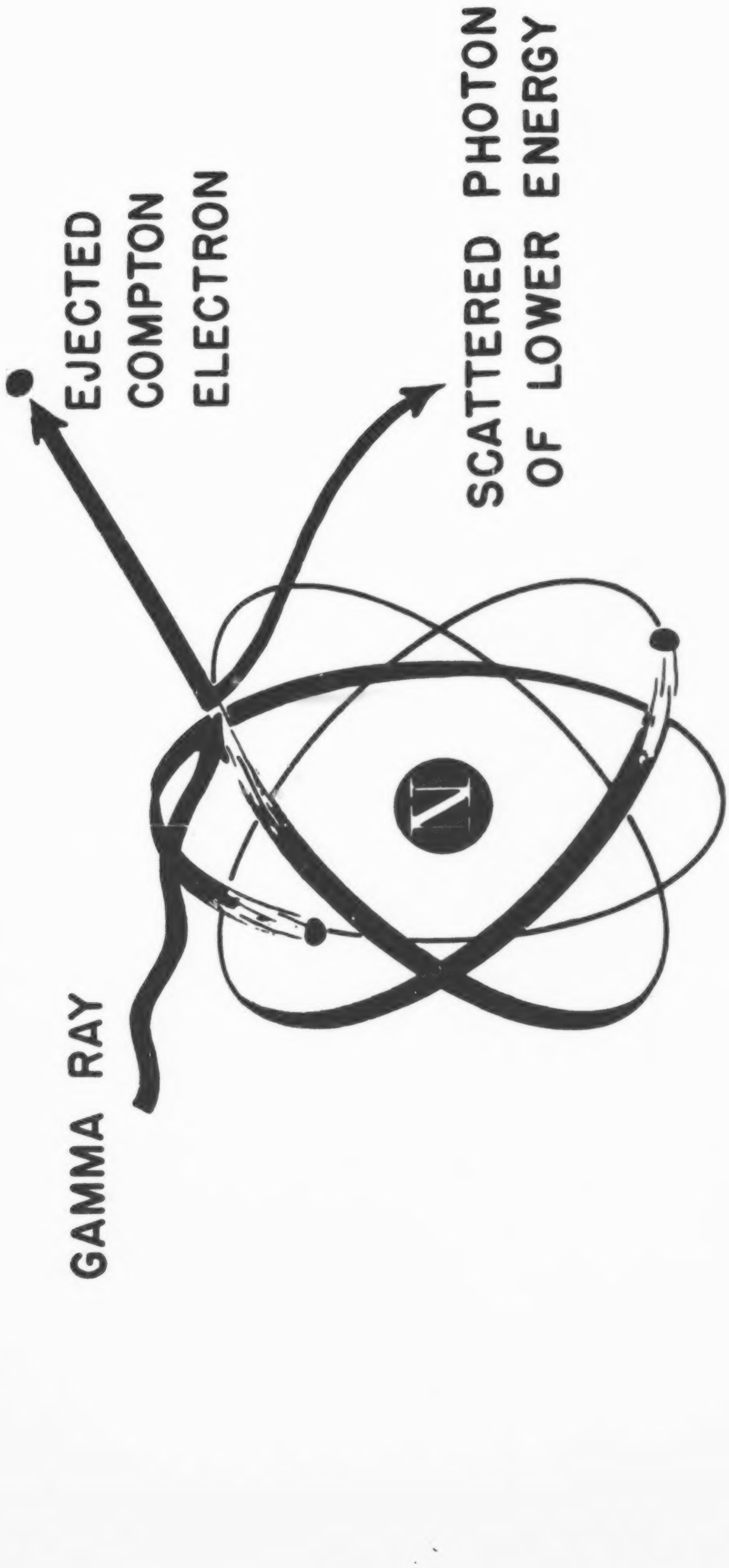
GAMMA RAY
EJECTED COMPTON ELECTRON
SCATTERED PHOTON OF LOWER ENERGY
N

Figure V-2.--Compton Effect
(Primarily Medium-Energy Photon)

Compton scattering involves the outer orbital electrons of an atom and does not produce characteristic x rays except in very special cases.

Theoretically, the Compton electron may receive any amount of energy up to a maximum value which is called the Compton edge.

$$\text{Compton edge} = E_\gamma - \frac{E_\gamma}{1+3.92\ E_\gamma}$$

where E_γ is the energy of the primary photon.

The remaining energy is carried away by the scattered gamma photon. The variable energies of the Compton electrons give rise to the "Compton continuum" in scintillation counting.

3. Pair Production

Pair production predominates when high-energy gamma photons interact with high atomic number absorber materials. Pair production is impossible unless the gamma ray possesses at least 1.02 MeV of energy (twice the mass energy of an electron). Practically speaking, it does not become important until 2 MeV in most absorbers.

In pair production, a gamma photon simply disappears in the vicinity of a nucleus. In its place, a pair of electrons appears--one negative, one positive (called a positron). The principal function of the nucleus is to allow conservation of momentum when the photon transfers its entire energy to the recoil particles. The negative and positive electrons are produced in order to conserve charge. Masses of these electrons have been created from the energy of the photon according to the familiar Einstein equation $E = mc^2$ where E is energy in ergs, m is mass in grams, and c is the velocity of light in cm/sec. Any photon energy in excess of the 1.02 MeV required to create two electron masses is simply shared between the two electrons as kinetic energy of motion, and they are ejected from the atom with high velocities.

In most instances, the electron and positron are ejected from the nucleus predominantly in the direction of the incident photon, especially when the photon energy, and hence its momentum, are very large.

The negative electron behaves in the ordinary way, producing secondary ion pairs until it loses all of its energy of motion. The positive electron also produces secondary ionization so long as it is in motion, but when it has lost its kinetic energy, it encounters a free negative electron somewhere in the material. The two are attracted by their opposite charges, and, upon contact, annihilate each other, converting the mass of each into pure energy. In order that energy and momentum again be conserved, the annihilation energy appears as two gamma photons of 0.51 MeV each, emitted at approximately 180° with respect to each other but randomly with respect to the incident photon direction. (See Figure V-3.)

The average lifetime of positrons in liquids and solids is 10^{-9} to 10^{-10}

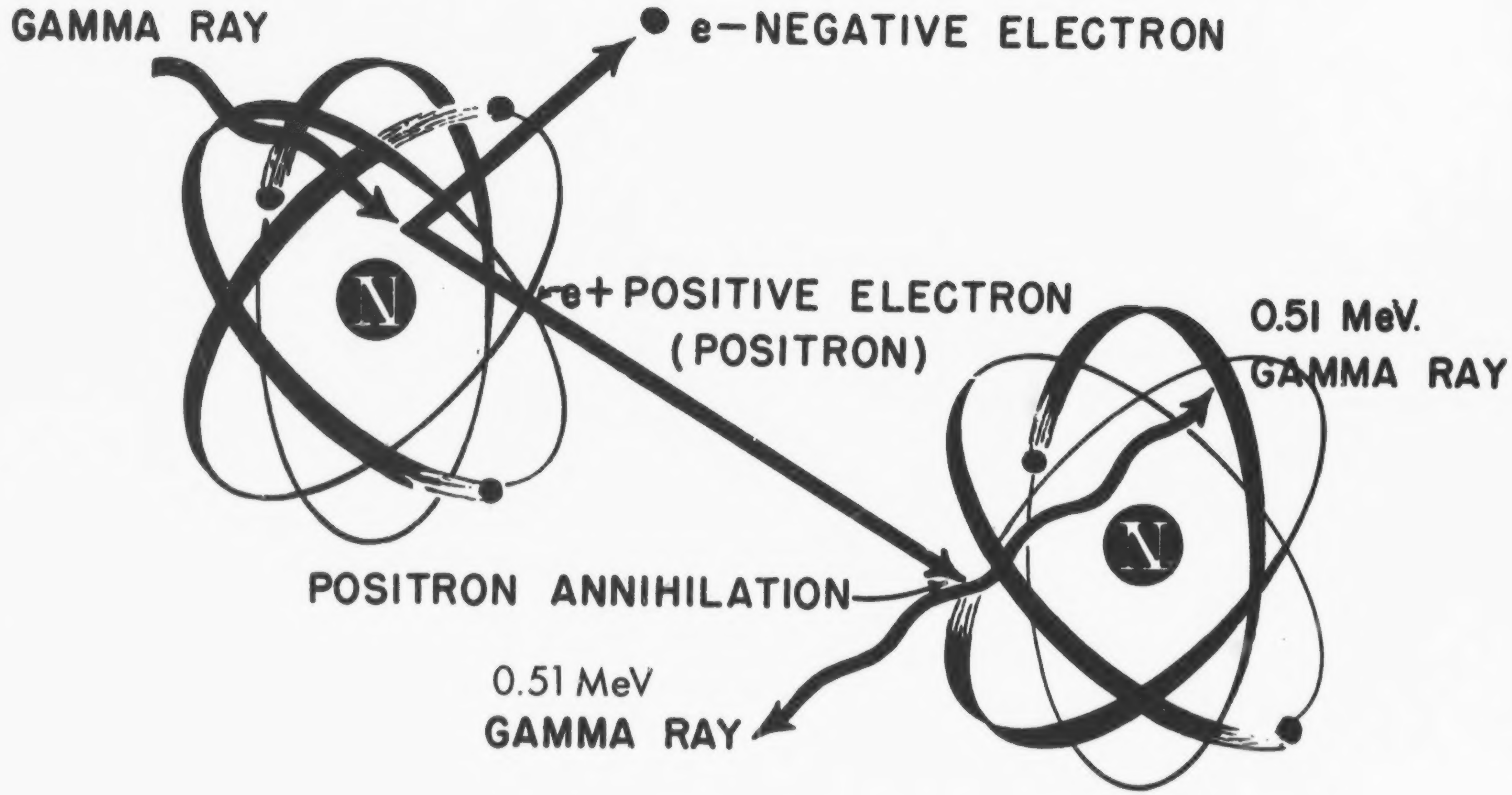
GAMMA RAY
e—NEGATIVE ELECTRON
e+POSITIVE ELECTRON
(POSITRON)
N
N
0.51 MeV.
GAMMA RAY
POSITRON ANNIHILATION
0.51 MeV
GAMMA RAY

Figure V-3.--Pair Production
(High-Energy Photon, > 1.02 MeV)

seconds. The ultimate fate of the annihilation gammas is either photoelectric absorption, Compton scattering followed by photoelectric absorption, or escape from the material.

Figure V-4 shows the fraction of the total decrease in photon beam intensity which is due to each mode of interaction for energies between 10 keV and 100 MeV, using lead as the absorbing material. At low energies, the photoelectric interactions predominate; at intermediate energies Compton scattering is the most likely interaction; and at high energies pair production is the most important. The ordinate of the curves in Figure V-4, "mass attenuation coefficient," is defined in chapter XV under Shielding. Suffice here to say that the higher the mass attenuation coefficient the greater is the probability that the radiation will interact in a unit mass of material.

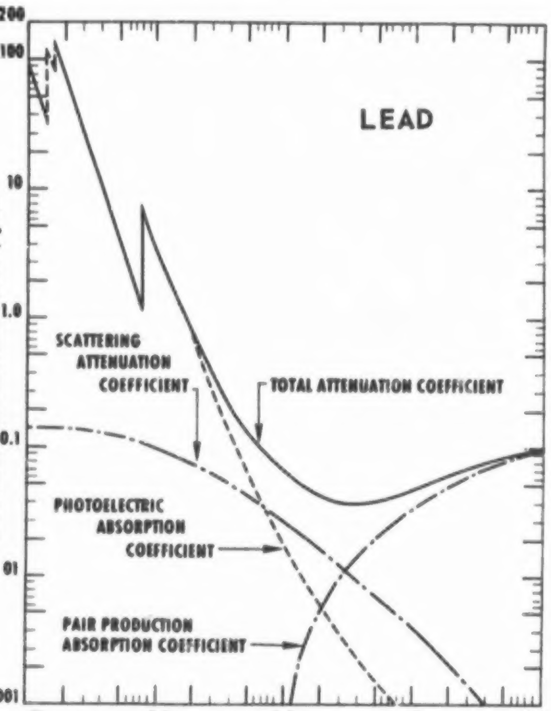

Figure V-4.--Mass Absorption Coefficients for Lead

V. SUMMARY

Alpha, beta, and gamma radiation interact primarily by ionizing and exciting the atoms and molecules of absorbing media. Alpha particles are highly ionizing and weakly penetrating; beta particles are intermediate in both specific ionization and penetrating power; gamma rays are very highly penetrating with subsequent low specific ionization.

Gamma rays interact with matter by three major processes; photoelectric effect (complete energy transfer), Compton effect (partial energy transfer), and pair production (complete energy transfer with production of annihilation photons). The photoelectric effect dominates at low gamma energies and high atomic number absorber materials; Compton effect predominates at intermediate energies and low atomic number absorber materials; and pair production is most important at high energies with high atomic number absorber materials. The rate of interaction of gamma rays per unit mass is dependent on the absorbing material and the gamma energy.

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CHAPTER VI

PRINCIPLES OF RADIATION DETECTION

I. INTRODUCTION

The detection and measurement of radiation must be accomplished by instruments, since man has not been provided with senses capable of responding to its presence.

All methods of detection are based on the ability of radiation to cause ionization; that is, to produce charged bodies from neutral atoms and molecules. Radiation measurement instruments vary only in the medium in which the ionization is permitted to take place and in the method by which this ionization is detected and indicated.

At present, there are eight major groups of radiation detectors:

1. Gas ionization
2. Scintillation media
3. Semiconductors
4. Photographic emulsions
5. Thermoluminescence
6. Chemical decomposition media
7. Radiophotoluminescence and optical density measurements
8. Calorimetry

Before describing the types of detectors listed, it will be useful to keep in mind the functions or purposes the detection instrument must fulfill. Of prime importance in nuclear medicine are those detectors that can be used in laboratory systems designed for in vitro and in vivo counting applications. From the above list these include gas ionization, scintillation, and semiconductor detectors. The remaining detector types find most application in radiation protection work--either personal monitoring or area survey.

II. GAS IONIZATION INSTRUMENTS

Although scintillation detectors are more widely used in nuclear medicine work, gas ionization instruments are discussed first for purposes of illustrating the principle of operation of a radiation detector. Analogies can then be drawn to other types of detectors.

A. Regions of Instrument Response

If a variable source of direct voltage is impressed across an enclosed volume of gas, the rate of the electrical charge produced in the gas by a constant source of radiation may be measured on an external meter. As the voltage is increased above zero, five regions of instrument response will be observed, as shown in Figure VI-1.

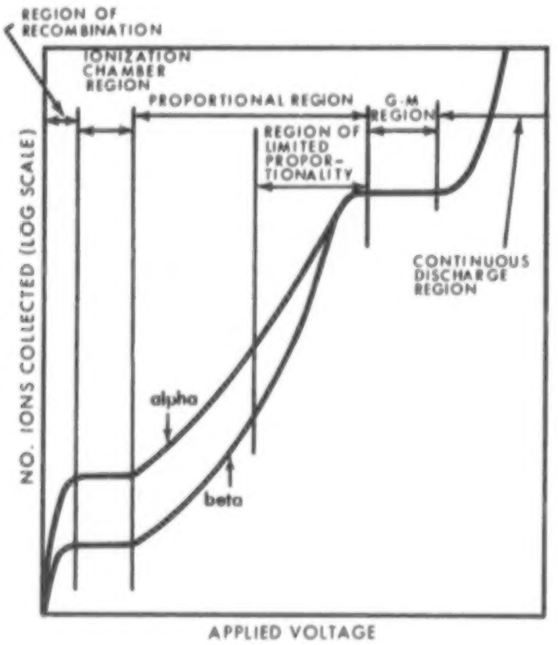

Figure VI-1.--Regions of Instrument Response

1. Region of recombination

In the first region, the ions produced by the radiation will be under very low voltage gradients and will tend to recombine with each other rather than migrate to the electrodes and be collected. This recombination of ion pairs decreases as the applied voltage is increased and finally becomes negligible; i.e., at some voltage the field strength will be sufficient to collect essentially all of the ion pairs that are formed. The first region is known as the region of recombination and is, with one or two rare exceptions, not useful for the operation of radiation detection instruments.

2. Ionization chamber region

The second region commences at the voltage at which all of the ions formed are collected. These ions are the primary ions resulting from the action of the radiation. The negative portion of the ion pair (electron) is accelerated toward the anode or positive electrode of the chamber, while the positive ion (residue of the atom) is drawn more slowly toward the cathode or negative electrode. For some large increment of voltage above the region of recombination, there is a saturation flow of ions which is equal to the number of ions produced by the radiation entering the chamber. This second region of operation is called the ionization chamber region, and provides the first of the three operating regions for gas ionization instruments.

3. Proportional region

If the voltage is increased still further, above the ionization chamber region, the collection of ions increases above the number collected in the previous region. This apparent anomaly (collecting more ions than are formed by the primary radiation) is the result of the increasing force applied to the electrons migrating to the anode of the chamber. When the voltage gradient is sufficiently high, the electrons achieve a high enough velocity to cause secondary ionization in the filling gas. This secondary ionization results in an amplification of the primary ion current produced by the radiation. Hence, each primary ion pair causes a magnified pulse of current. The number of secondary ions produced for each primary ion pair formed by the radiation is called the gas amplification factor. As the voltage is raised the gas amplification factor is increased. Gas amplification factors as high as 10^5 or 10^6 are sometimes employed in this region. The size of the pulse produced is proportional to the voltage applied across the gas and to the number of primary ion pairs formed. Thus an alpha particle with its high specific ionization will produce a much larger pulse of current than will beta radiation with its correspondingly lower specific ionization. This makes possible the discrimination among radiation types that differ in the produced primary ionization. This proportionality of current pulse size to impressed voltage and to ionization density results in the naming of the second region of instrument operation, the region of proportionality. The upper portion of this region where the alpha and beta curves begin to approach each other (see Figure VI-1), is referred to as the region of limited proportionality and it is not of general use in radiation instrumentation.

4. Geiger-Mueller region

With a further increase in operating voltage above the region of proportionality, a further increase in gas amplification occurs. This is due to the additional acceleration provided the electrons, and results in a veritable avalanche of electrons around the anode of the chamber. In this operating region, the counting rate produced by the avalanche is relatively independent of applied voltage over a limited range, and also is independent of the specific ionization of the initiating particle or photon. This third operating region is called the Geiger-Mueller region. Instruments operating in the Geiger-Mueller (G-M) region provide a gas amplification factor of as high as 10^{10}. The G-M region is extremely sensitive to any radiation that produces even one ion pair, and consequently, individual ionizing events can be detected.

The positive ions produced in the G-M tube migrate to the cathode where their electron deficiency is satisfied by the excess negative charge existing at the cathode. When the vacant orbits of the gas atoms are filled, electromagnetic radiation is emitted. This radiation, which may take the form of either ultraviolet or x radiation, tends to continue the discharge action, and so sustains the period during which the gas is essentially a conducting medium. In order to squelch this discharge action, a second agent is added to the primary gas. The secondary agent, called a quenching vapor, usually consists of polyatomic molecules (such as amyl acetate or ethyl alcohol) which, upon absorbing radiation, dissociate into particles not small enough to continue the avalanche action. More recently, halogen gases have received widespread use as quenching agents. These have the advantage that the molecules will recombine after dissociation thus increasing the useful life of the detector.

5. Region of continuous discharge

If the voltage is increased above the G-M region, the gas arcs thereby producing a state of continuous discharge. Sustained operation in this region may result in the ruination of the detector.

B. Operational Characteristics

Of the five regions of instrument response, there are three that can be used for specific purposes in radiation detection. The first, the ionization chamber region, provides low sensitivity but high range, since it measures only the primary ionization produced. Sensitivity is defined as a factor which is proportional to the response of an instrument to the type and energy of the radiation being measured. Discrimination among the several types of radiation is usually not possible with ionization chambers except by use of external absorbers. Operating voltage for ionization chamber instruments will usually be between 60 and 300 volts, depending upon the size of the chamber and the filling gas (usually air at atmospheric pressure).

Proportional instruments provide a high sensitivity due to their gas amplification and a correspondingly high range since the secondary ionization takes place over only a portion of the chamber volume. Due to the proportionality factor which exists in this region, the instrument is inherently capable of discriminating among the different types of radiation. Proportional counters are usually filled with argon, methane, or a mixture of the two, although air is sometimes used. Operating voltages will range from 500 to 5,000 volts, depending upon chamber design and filling gas.

The G-M region provides an extremely high sensitivity and a correspondingly low range due to the discharge dead time; i.e., the time during which the gas is conducting and hence is insensitive to any further ionizing events. Because of the nature of the discharge in G-M detectors it is impossible to discriminate electronically among the several types of radiation. Geiger-Mueller chambers are usually filled with argon or helium and a quenching vapor at lower than atmospheric pressure and operate in the range of 1,000 to 3,000 volts.

Each of the regions provides certain operating characteristics, as described above, which make it useful for one purpose or another. The ionization chamber region, providing a direct indication of the number of ions produced by a given radiation, is eminently suitable for indicating cumulative exposure or radiation exposure rate in Roentgen units. The low sensitivity and corresponding high range of ionization chambers make them useful for measuring levels of activity much higher than can be measured with the other types of detectors. Proportional instruments find their best use in the discrimination between alpha and beta-gamma radiation, while G-M instruments provide extremely sensitive indicating devices for measuring low intensities of radiation. Both the proportional and the G-M instruments are counters; that is, they provide a pulse of current for every particle or photon that interacts within the chamber. Ionization chambers may be designed as either pulse counters or current measuring devices.

III. SCINTILLATION DETECTORS

In recent years one of the most rapidly developing fields in radiation detection instruments has been that involving the use of scintillation media. Although scintillation detectors have been in use since the early 1900's, the upsurge in their application occurred in the early 1950's following the improved design of photomultiplier tubes and increased availability of scintillation media. At present scintillation detectors are used more extensively than any other type in nuclear medicine laboratories.

A. Principle of Operation

The basic parts of a scintillation detector are shown in Figure VI-2. The sensitive part of the detector is the phosphor.

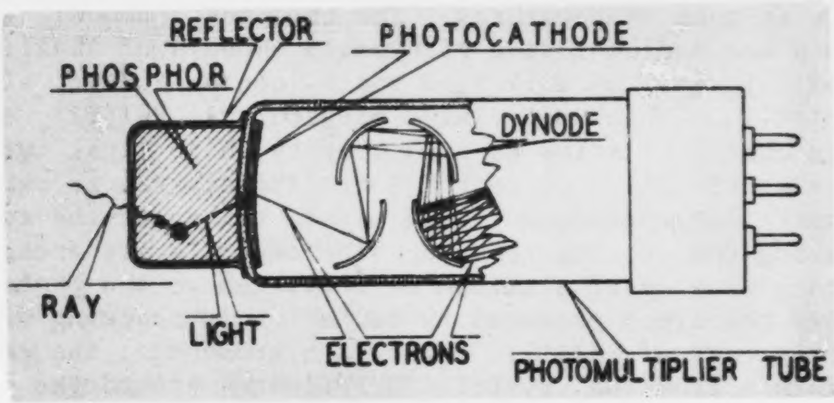

Figure VI-2.--Scintillation Detector

Energy from the radiation is transferred to the phosphor via the various types of interactions which were discussed previously. Some fraction of the transferred energy is re-emitted by the phosphor as visible light, the intensity of which is proportional to the amount of energy which was transferred from the photon or particle to the phosphor. The light is transmitted through the phosphor to the light-sensitive cathode of a photomultiplier tube causing electrons to be ejected from the cathode. The ejected electrons are focused onto the first of nine or ten secondary electron-emitting electrodes called dynodes which are maintained at a positive potential with respect to the cathode. A gradient of approximately 100 volts is maintained between each dynode. The dynodes are shaped so that the electrons ejected from one are focused onto the next.

The electrons ejected from the last dynode are collected on an anode and brought out of the tube as a pulse of current. The ratio of the number of electrons ejected from a given dynode to the number ejected from the preceding one is called the secondary emission ratio. This ratio ranges from 2 to 7 depending on the coating on the dynode and the energy of the bombarding electron. The total multiplication factor for a ten dynode photomultiplier tube then, is the secondary emission ratio raised to the 10th power.

Since the output current from the photomultiplier tube is proportional to the light incident on the photocathode, which is in turn proportional to the energy transferred from the radiation to the phosphor, scintillation detectors are well suited to energy spectrum analysis. The use of scintillation detectors in spectroscopy systems is discussed in chapter VIII.

B. Types of Phosphors

1. Inorganic crystals

Inorganic crystals are in most widespread use as gamma-ray detectors and comprise the majority of the scintillation detectors used in nuclear medicine laboratories. Inorganic crystal scintillators are crystals of inorganic salts, primarily the alkali halides, containing small amounts of impurities called activators which cause the crystal to scintillate at room temperatures. The ones most commonly used as gamma detectors are sodium iodide with small amounts of thallium as the activator [NaI(Tl)] and, on a limited basis, cesium iodide, also thallium activated [CsI(Tl)]. These materials, particularly NaI(Tl) exhibit such desirable characteristics as high density, high light output, transparency, and suitable index of refraction. The crystal is carefully grown in a controlled environment with minute traces of the activator introduced during the growing process. The crystals are encased in light-tight cans usually of aluminum or beryllium so the photomultiplier tube views only the light produced by radiation interacting within the crystal. In the case of NaI(Tl), which is hygroscopic, the casing also seals out moisture from the crystal. A reflector around the crystal serves to maximize the light collection by the cathode of the photomultiplier tube. (See Figure VI-2.)

2. Organic crystals

Organic crystals as scintillation detectors have been used primarily for counting beta particles where the high atomic number of the inorganic crystals causes excessive scattering of the particle within the detector. Of the many organic crystals which have been studied to date, the most useful are anthracene and transstilbene. Organic crystal detectors have found little application in nuclear medicine where much work is done with low energy beta emitters, carbon-14 and tritium. Liquid scintillation detectors are better suited to such applications than are organic crystal scintillators.

3. Liquid organic scintillators

The need to count the low energy beta particles from carbon-14 and tritium led to the development of organic liquid scintillation detectors. The advantage of these being that the sample can be dissolved (or mechanically suspended) in a solvent containing the organic phosphor. Hence the absorption problems associated with other types of radiation detectors are largely eliminated. Phosphors used in liquid scintillation detectors include p-terphenyl, 2,5 - diphenyloxazole (PPO), and 2,5 - bis - 2(5-t-Bulyl-benzoxazolyl) - Thiophene (BBOT). Solvents in general use are aromatic hydrocarbons or aromatic ethers, although other compounds are used where solubility is a factor.

Liquid scintillators now constitute a very important class of radiation detectors in nuclear medicine laboratories, and especially in biochemical research applications. The use of liquid scintillation detectors in systems which utilize coincidence circuitry and low temperatures to achieve low backgrounds for counting low-energy beta particles is discussed in Chapter VIII.

4. Other types of phosphors

Other scintillation media that have been used as radiation detectors include plastic phosphors for beta counting and inorganic powders which are used primarily as alpha detectors. An example of the latter is zinc sulfide powder activated with silver which is coated directly on the glass envelope of a photomultiplier tube or on a transparent material such as lucite. These types of detectors are not in widespread use in nuclear medicine.

IV. SEMICONDUCTORS

The state of the art of semiconductor radiation detectors has advanced rapidly in recent years. The most widely used types of semiconductor devices are diffused p-n junction, surface barrier, and lithium drifted detectors. Semiconductor detectors have so far found most application in the field of particle spectroscopy, although lithium drifted detectors are now being used as gamma detectors.

A. Diffused p-n Junction

The diffused p-n junction detector obtains its name from its manufacturing process. A slice of p-type silicon or germanium crystal with a layer of n-type impurity (usually phosphorus) deposited on the surface, is heated to form a p-n junction just below the surface. The phosphorus may also be painted onto the silicon and made to diffuse into it by applying heat. Since the n-type material has an excess of electrons and the p-type has an excess of "holes" (holes may be thought of as unit positive charges), the natural action of the combined materials tends to align the electrons on one side of the junction and the holes on the other. Thus a difference of potential is built up across the junction.

By applying an external voltage to the crystal of such polarity as to oppose the natural movement of electrons and holes (reverse bias) the potential barrier across the junction is increased and a "depletion region" is produced. (See Figure VI-3.)

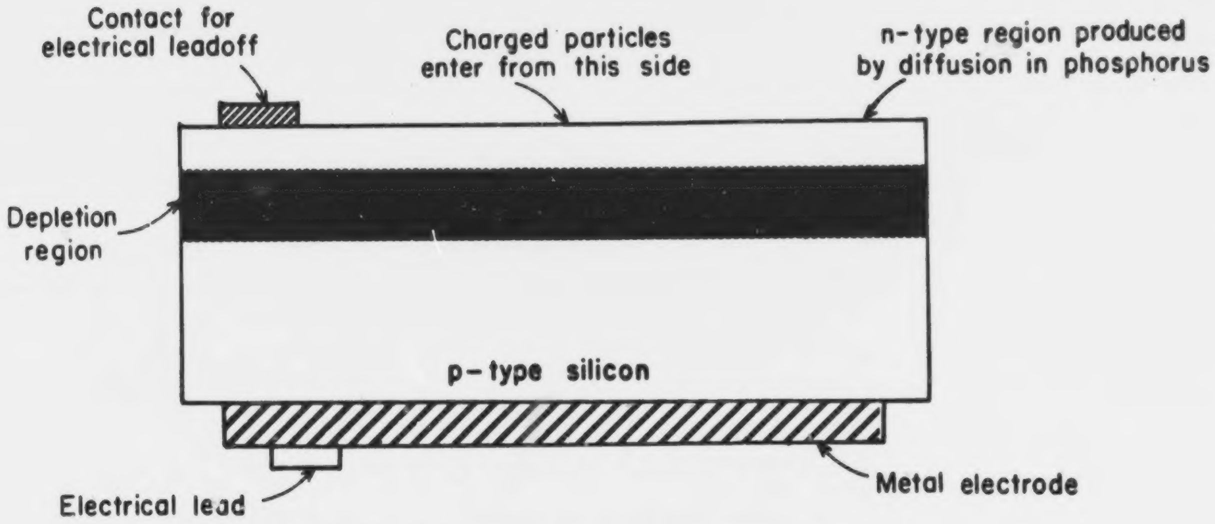
Contact for electrical leadoff
Charged particles enter from this side
n-type region produced by diffusion in phosphorus
Depletion region
p-type silicon
Electrical lead
Metal electrode

Figure VI-3.--Schematic Representation of a Diffused p-n Junction Detector

This depletion region is the sensitive volume of the detector and is analogous to the gas volume in a gas ionization detector. Charge particles upon entering the depletion region produce electron-hole pairs analogous to ion pairs produced in gas ionization chambers. Since an electric field exists in this region, the charge produced by the ionizing particle is collected thus producing a pulse of current. The size of the pulse is proportional to the energy expended by the particle.

B. Surface Barrier Detectors

The principle of operation of the surface barrier and lithium drifted detectors is the same as for the p-n junction in that a depletion region, in which there exists an electric field, is produced. The method of producing the depletion region as well as its dimension and location within the crystal vary from one type of detector to another.

The surface barrier detector depends upon the surface states of the silicon or germanium for its operation. At the surface of a piece of pure crystal an electric field exists such that both holes and electrons are excluded from a thin region near the surface. For n-type crystals the field is such as to repel the free electrons from this region. If a metal is joined to the crystal the free electrons are still repelled, but a concentration of holes is produced directly under the surface. Then if a reverse bias is applied, a depletion region is produced. (See Figure VI-4.)

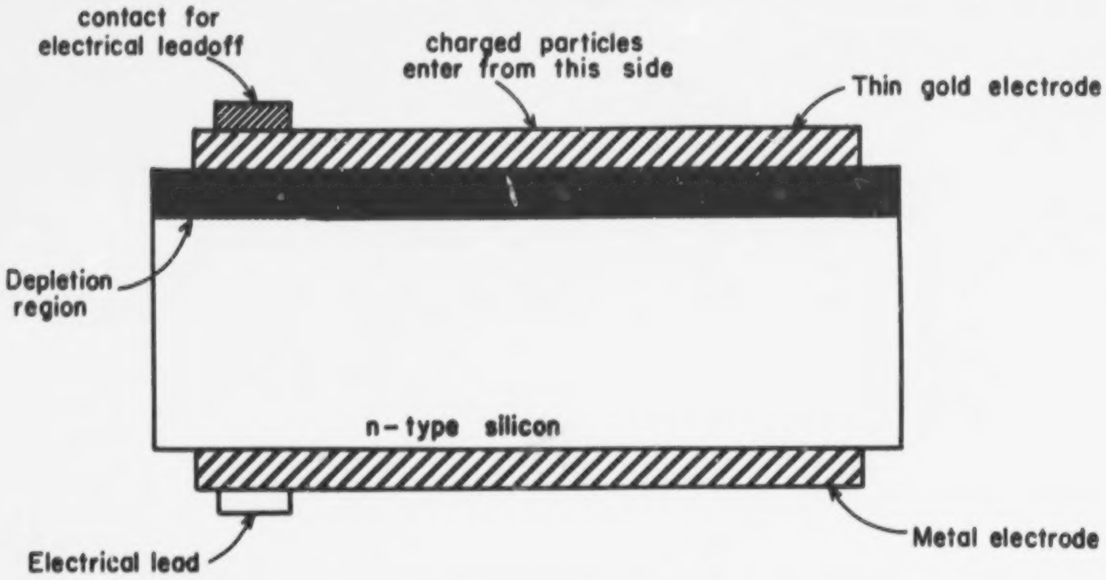

Figure VI-4.--Schematic Representation
of a Surface Barrier Detector

Surface barrier detectors give better resolutions for particle spectroscopy than p-n junctions, but wider depletion regions are possible with the latter. (The wider the depletion region, the higher the energy of particles which can be analyzed since the particle must expend all its energy in the depletion region.)

C. Lithium Drifted Detectors

The lithium drifted detector is produced by diffusing lithium into low resistivity p-type silicon or germanium. When heated under reverse bias, the lithium ions, which serve as an n-type donor, drift into the silicon or germanium in such a way that a wide layer of the p-type material is compensated by the lithium so that the effective resistivity is comparable with that of the intrinsic material. (See Figure VI-5.) Wider depletion regions can be obtained by the lithium drift process than by any other known method. Consequently lithium drifted detectors show the most promise for gamma spectroscopy work. Silicon detectors can be operated at room temperatures, but exhibit low efficiency for gamma rays. Germanium detectors have higher gamma efficiencies, but must be operated at liquid nitrogen temperatures. For these reasons, coupled with the small sensitive volumes obtainable to date, semiconductor detectors have not received widespread application in nuclear medicine. Much work is being done, however, to develop semiconductor detectors that are practical for in vivo gamma measurements since the inherent resolution for spectroscopy work is much superior to that obtainable with sodium iodide.

V. PHOTOGRAPHIC EMULSIONS

Darkening of a photographic plate by radiations emanating from radioactive material was the first method used to detect nuclear radiation. The use of photographic films for radiation measurement is at present confined mostly to monitoring exposed personnel and conducting

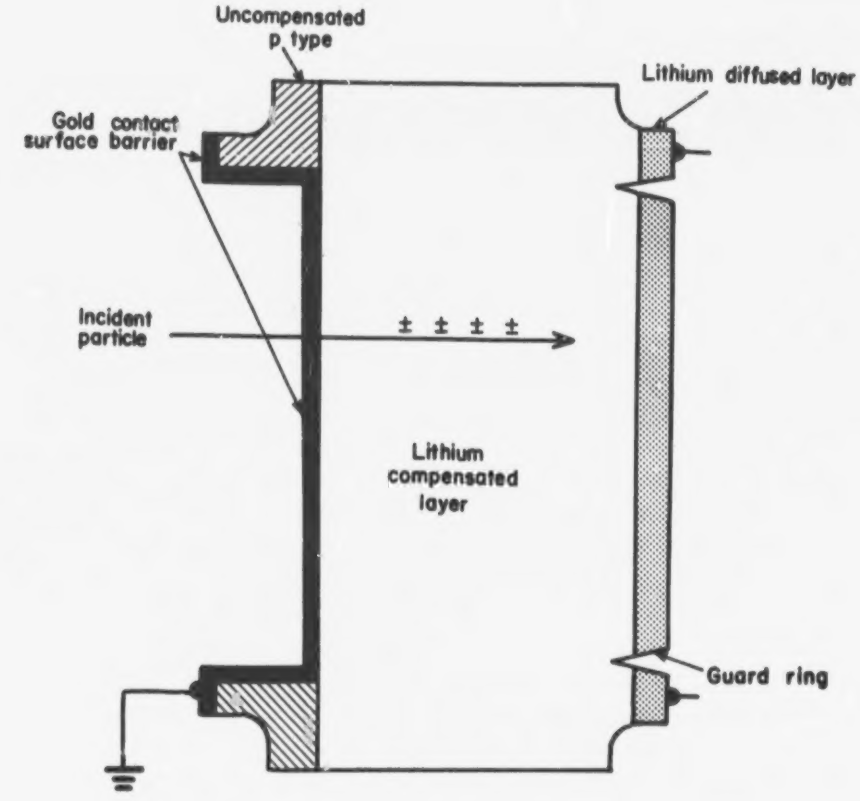

Figure VI-5.--Schematic Representation of a Lithium Drifted Detector

area surveys. Films are also used in research work in making radioautographs of cosmic rays or substance containing radioactive materials. The mode of interaction of radiation with the silver halide in an emulsion is that of ionization. After an emulsion has been exposed to radiation, there is no visible sign of any change, but upon development, the latent image is converted into a black deposit of metallic silver. The extent of film darkening may be related to the type, energy, and quantity of radiation to which the film was exposed.

VI. THERMOLUMINESCENCE

Thermoluminescence is the phenomenon by which certain crystals are able to store energy transmitted to them by radiation and then emit this energy in the form of visible light upon heating. Almost any insulating transparent material exhibits this property. Crystals commonly used are lithium flouride and calcium flouride. The centers of energy storage or "sensitivity centers" are probably imperfections in the crystalline structure; either structural defects or foreign impurities in the crystal. Electrons freed by the ionizing radiation are trapped at the sensitivity centers until released by heat supplied to the crystal. When the trapped electrons are released, light is emitted of an intensity proportional to the energy transferred to the crystal from the radiation.

Thermoluminescent dosimetry shows much promise for the future in the areas of personnel monitoring and radiation research. Its advantages include wide operational range (5 mrads to 2 × 10^5 rads), simplicity, ease and speed in reading, its reusability, and the response can be made relatively independent of energy from 40 keV to 1.25 MeV.

VII. CHEMICAL DECOMPOSITION INDICATOR

In chemical decomposition indicators, ions produced by radiation combine chemically to form new compounds or change the chemical characteristics of a compound.

A typical chemical decomposition indicator is a chloroform-water mixture which, when exposed to radiation, produces hydrochloric acid in proportion to the amount of radiation absorbed. This formation of acid decreases the pH, and, by the use of a suitable indicator, it is possible to ascertain when a predetermined dose has been received by the chemical system. An indicator frequently used for this purpose is brom-cresol-purple.

An inherent drawback of chemical decomposition indicators is the low sensitivity. It requires exposures of the order of 25 roentgens before detectable chemical changes are induced. Consequently, these detectors are best suited for measuring the dose from large sources of radiation or for civil defense monitoring purposes.

VIII. RADIOPHOTOLUMINESCENCE AND OPTICAL ABSORPTION

Radiophotoluminescence is the phenomenon by which certain materials undergo changes in their photoluminescent properties subsequent to irradiation. Irradiated material will fluoresce when activated by light of the proper wavelength (ultraviolet or near ultraviolet), whereas unirradiated material will not fluoresce under the same conditions.

Silver-activated phosphate glass has proved useful as a radiation detecting medium exhibiting the radiophotoluminescence property. The ionizing radiation liberates electrons within the glass which are trapped by the Ag^+ ions of the glass. The resulting metallic silver centers serve as the origin of the photoluminescence. After radiation exposure of the glass it is subjected to ultraviolet light and the resulting fluorescence is detected by means of a photomultiplier tube. The intensity of the light emitted is proportional to the dose which the glass received. Personnel dosimeters of this type have been developed which cover the range from 10 to 600 rads.

Higher radiation doses may be determined by measuring the increased optical density of the glass after irradiation. This is done by making optical transmission measurements using light of the proper wavelength for the dose range of interest. This principle is useful from 10^3 to 10^6 rads.

IX. CALORIMETRY

Calorimetry takes advantage of the heating effect of radiation. A calorimeter is a device used to measure quantities of heat. Calorimeters provide a means of measuring directly the energy absorbed in a medium as a result of exposure to radiation. Calorimetry can also be used to determine the activity of a large quantity of radioactive material.

The main advantage of the calorimetric method for measuring absorbed energy or activity is its inherent accuracy. For dosimetry purposes a direct reading of energy absorption can be obtained. However, the rate of heat input is so small that only very high intensities of radiation can be measured. For this reason calorimetry is not used for routine monitoring purposes. Applications include the measurement of the activity of curie amounts of alpha emitters and the measurement of the energy of particles produced by particle accelerators.

X. SUMMARY

Of the many different media used as radiation detectors, the sodium iodide crystal is at present the most widely used in nuclear medicine since most of the work involves the detection of gamma radiation. Personnel monitoring devices employing photographic films and thermoluminescent media are used to monitor personnel exposure. Gas ionization instruments and liquid and solid scintillators are preferred for alpha and beta counting. Other principles of detection such as radiophotoluminescence and calorimetry may be employed where very high levels of radiation are present.

SUGGESTIONS FOR FURTHER READING

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2. Quimby, E.H. and Feitelberg, S., Radioactive Isotopes in Medicine and Biology, Lea and Febiger, Vol. 1 (1965), chap. 12.

3. Blahd, W.H., Nuclear Medicine, McGraw-Hill Book Co. (1965), pp. 25-42.

CHAPTER VII

LABORATORY COUNTING SYSTEMS
I. Integral Counters

I. INTRODUCTION

None of the radiation detection devices discussed in the previous chapter, will, in themselves, enable one to make accurate reliable measurements in the laboratory. That is, they must be incorporated into a total counting system which consists of various and sundry electronic components. The number and types of electronic accessories vary with the type of counting system and the job it is to perform. The systems discussed in this chapter are those that register all ionizing events that result in an electrical pulse greater in magnitude than a certain threshold value. These systems are referred to as integral counters. Differential or window counting and spectroscopy, which are accomplished by means of pulse height analysis, are discussed in Chapter VIII.

II. GAMMA SCINTILLATION COUNTERS

Figure VII-1 shows a block diagram of a typical integral gamma counting system. Photons interacting in the NaI(Tl) crystal cause light flashes which are converted to electrical pulses. The pulses are amplified and counted by means of the associated electronic components.

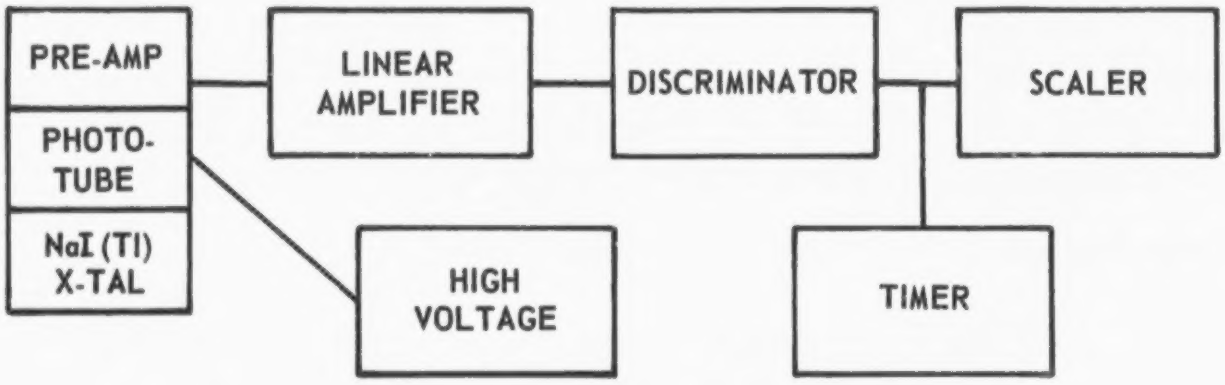

Figure VII-1.--Typical Laboratory System for Integral Gamma Counting

A. Detector Assembly

The basic parts of the detector, as shown in Figure VII-2, are the scintillation crystal, the reflector, the crystal container, and the photomultiplier tube, one part of which is the photocathode.

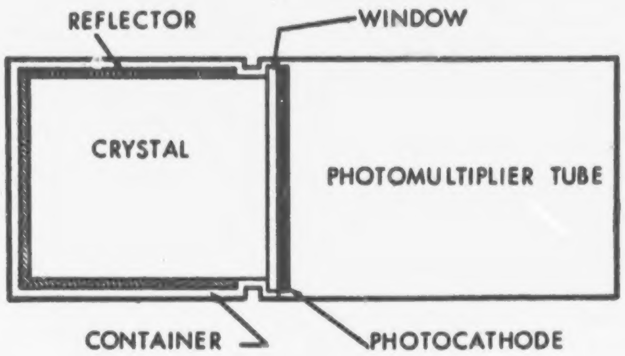

Figure VII-2.--Schematic Diagram of a Scintillation Detector

1. The crystal

The sensing unit of the spectrometer is the crystal. It is especially chosen for its ability to produce scintillations when photons interact within its structure. The most common choice of crystals for gamma-ray detection is the sodium iodide, thallium activated, [NaI(Tl)] crystal. The crystal is carefully "grown" with minute traces of a specific impurity known as an "activator" introduced during the growing process. The activator causes the crystal to scintillate at room temperature when energy is supplied to it from an external source. Crystals are encased in light tight cans usually of aluminum or beryllium. The encasement is necessary so that the only light viewed by the photomultiplier is that produced by radiation interacting within the crystal. The reflector surrounding the crystal serves to maximize the light getting to the photocathode per unit of energy absorbed in the crystal. The crystal is usually surrounded by lead shielding to reduce background radiation.

In the case of NaI(Tl) crystals it is important that the crystal be permetically sealed to keep out moisture. The sodium iodide is hygroscopic and collects moisture if exposed to the atmosphere. If water droplets form on the crystal they will gradually dissolve it.

2. Interaction in the crystal

With detectors constructed as shown in Figure VII-2 it is apparent that the canning will prohibit charged particulate radiation from reaching the crystal. Thus, interactions within the crystal are due solely to gamma or x radiation. Photons, on entering the crystal, can either interact or pass through undisturbed. Although many photons do pass through undisturbed, a significant number interact with the crystal atoms. It is important to recall that gamma- and x-ray photon interactions with matter occur primarily by three modes: photoelectric effect, Compton scattering, and pair production. In each of these interactions photon energy is imparted to either an electron or a positron. It is the movement of these charged particles through the crystal lattice, exciting the atoms and molecules, that initiates the scintillation process.

The crystal atoms receive energy from a speeding charged particle passing nearby. The energy transfer slows the passing particle slightly. The atom absorbs the energy by increasing the energy state of one or more of its more loosely bound electrons. Since these electrons cannot exist very long in this excited state they will quickly release the excess energy by emitting a light photon and return to a more stable energy state. The light output of one flash is in reality the total of millions of such events occurring within approximately 10^{-12} seconds.

Of the three primary photon interactions discussed below--viz., photoelectric, Compton, and pair production--only photoelectric and Compton interactions are of notable importance in nuclear medicine work, since pair production occurs only at photon energies greater than 1.02 MeV.

The photoelectric process is one in which the total photon energy is transferred directly to an orbital electron. Although the photoelectron may cause secondary ionization, the freed electrons will be slowed down and will give up their energy through excitation processes to produce light. These events happen so quickly that they appear as a single flash of light representative of the entire energy of the photon.

The Compton scattering process results in only a portion of the photon energy being imparted to the orbital electron. The scattered photon with reduced energy may escape from the crystal or it may interact elsewhere in the crystal and undergo a photoelectric or another Compton scattering process. If both the initial and the scattered photons interact in the crystal, the processes occur so quickly that again it appears as one event of total energy transfer.

In the pair production process, 1.02 MeV of the incident photon energy is converted to mass in the form of an electron and a positron. The remainder of the photon energy is divided between the two particles as kinetic energy. The positron, upon slowing down, combines with an electron and the two particles annihilate, thus producing two photons of 0.51 MeV energy each. Either one or both of these photons may interact in the crystal by the former processes (see above). Again the chain of events appears as one event. If both photons interact in the crystal, the scintillation is indicative of the total initial photon energy ($E\gamma$). Since there is also a probability that one or both of the photons from the positron annihilation will escape from the crystal, the light intensity may be indicative of one escaping photon ($E\gamma$-0.51 MeV) or two escaping photons ($E\gamma$-1.02 MeV).

3. The photomultiplier tube

The light energy produced in the crystal is converted into electrical energy by means of the photomultiplier tube which is composed of a photocathode and an electron multiplier. The photocathode, upon being struck by light, emits electrons. The number of electrons released is proportional to the amount of light incident upon the photocathode. The small number of electrons released is then multiplied by accelerating them across a series of voltage potentials. (See Chapter VI.) The result is an electrical pulse at the output of the photomultiplier tube whose size (height) is proportional to the energy absorbed in the crystal.

An external unit, the high voltage power supply, is used to furnish a large voltage potential to the photomultiplier tube. The power supply can be either a battery pack or an electronic instrument which will deliver a preselected voltage between 500 and 2,000 volts. The power supply must be very stable since small variations in the applied voltage may result in significant errors in the accumulated data.

B. Preamplifier

Although there exists at the output of the photomultiplier tube an electrical pulse, it is still weak and could be easily lost if transmitted over any significant length of cable. In order to maintain a reliable flow of information a preamplifier is installed close to the photomultiplier tube to shape and strengthen the signal for the trip to the remainder of the system.

C. Linear Amplifier

The function of the linear amplifier is to amplify the pulses from the preamplifier in a linear fashion, i.e., each pulse must be amplified by the same factor no matter what its original height. A good linear amplifier will accomplish this over a wide range of pulse magnitudes without distorting the shape of the pulse. The amplification factor is called the gain of the amplifier. In some integral counting systems an external gain control is provided, but many have a fixed gain which must be adjusted internally.

D. Pulse Height Spectrum

In order to understand the operation of the next component of the system, the discriminator, it is necessary to know what is meant by "pulse height spectrum."

Each electrical pulse that exists at the output of the linear amplifier is proportional in height (pulse height refers to the magnitude of the signal in volts) to the energy deposited in the NaI crystal by the interacting photon. Thus a linear relationship exists between pulse height and absorbed energy.

Consider now the relative pulse height distribution one would expect if gamma rays from ^{137}Cs, which are monoenergetic (662 keV), were allowed to interact with a NaI crystal. Those photons which interact by the photoelectric effect are completely absorbed and yield a pulse representative in height of the 662 keV of energy absorbed. These pulses are represented in Figure VII-3 as having a relative pulse height of approximately 5 units. All of these pulses are approximately the same height but not exactly so, because statistical processes within the system result in a distribution of pulse heights for a given amount of energy absorbed in

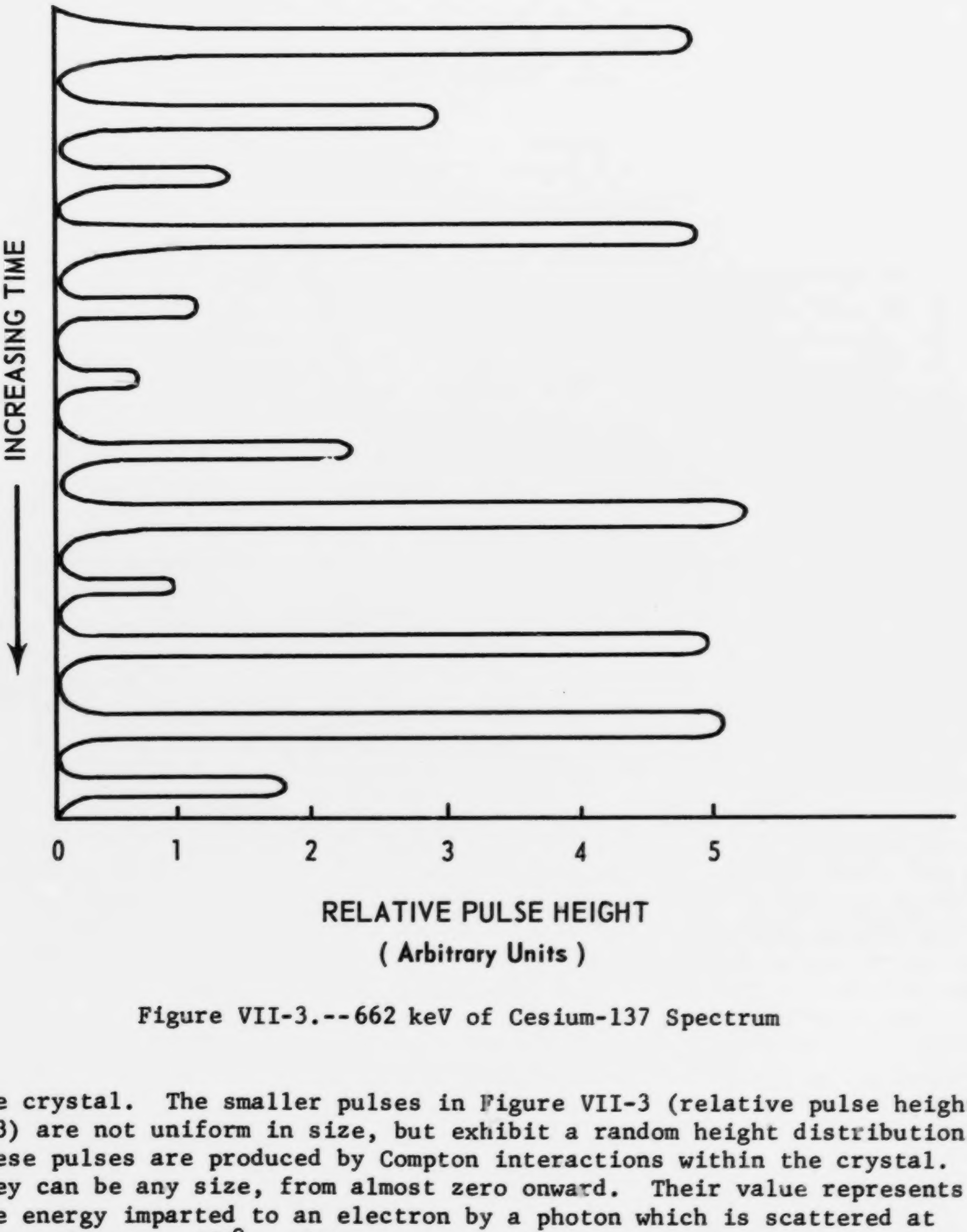

Figure VII-3.--662 keV of Cesium-137 Spectrum

the crystal. The smaller pulses in Figure VII-3 (relative pulse heights 1-3) are not uniform in size, but exhibit a random height distribution. These pulses are produced by Compton interactions within the crystal. They can be any size, from almost zero onward. Their value represents the energy imparted to an electron by a photon which is scattered at any angle up to 180°. This energy, called the "Compton edge," is represented by an arbitrary pulse height of 3 units in Figure VII-3.

If the number of pulses of a given size are plotted against pulse height for a given counting time the distribution shown in Figure VII-4 results. The horizontal axis could be labeled in energy units since it is known in this example that a relative pulse height of 5 represents 662 keV. This

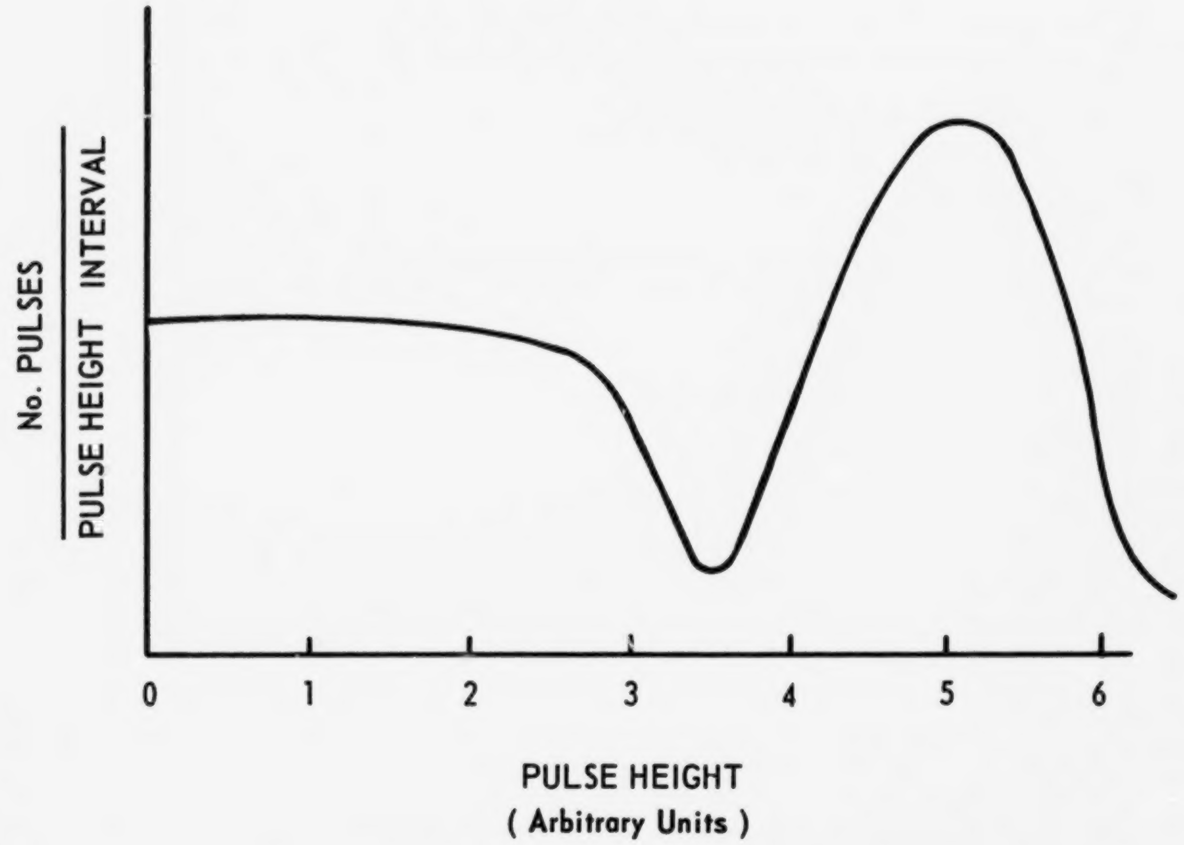

Figure VII-4.--Pulse Height Spectrum

type of presentation is called a "pulse height spectrum" or "gamma energy spectrum." The dip in the spectrum between 3 and 4 units is called the "Compton valley" and is caused by the gap which exists between the maximum Compton energy and the actual photon energy. Actually there would be no pulses between 3 and 5 were it not for the statistical phenomena previously mentioned. The part of the spectrum that represents total photon energy absorption (approximately 5 units) is called the "photopeak." For a given energy photon the relative position of the photopeak along the horizontal axis can be controlled in two ways: by varying the voltage applied to the photomultiplier tube and by adjusting the gain of the linear amplifier.

E. Discriminator

The discriminator is a device that electronically blocks out pulses smaller than a certain size. In integral counting systems a single discriminator is used, and all pulses larger than a predetermined level are transmitted by the discriminator to a readout device. For most counting applications it is best to set the discriminator in the Compton valley, i.e., only photopeak pulses are counted. There are two reasons for this: first, scattered photons may represent unwanted information (although this is not always true as will be seen in Chapter XII) and, secondly, the Compton valley is the point on the spectrum where the integral counting rate is changing least rapidly; thus minimizing errors due to slight shifts in the spectrum. Figure VII-5 illustrates the proper discrimination level for the hypothetical ^{137}Cs spectrum. This arrangement results in the rejection of all pulses with a relative pulse height less than about 3.5 units; consequently, only those pulses arising from total absorption of the primary photons are recorded along with the ever present background pulses. Some integral counting systems have a "fixed" discrimination level, i.e., the discriminator setting cannot be adjusted externally. In such systems, one, in effect, sets the discrimination level by means of the high voltage and/or amplifier gain controls which change the position of the spectrum relative to the fixed discrimination level.

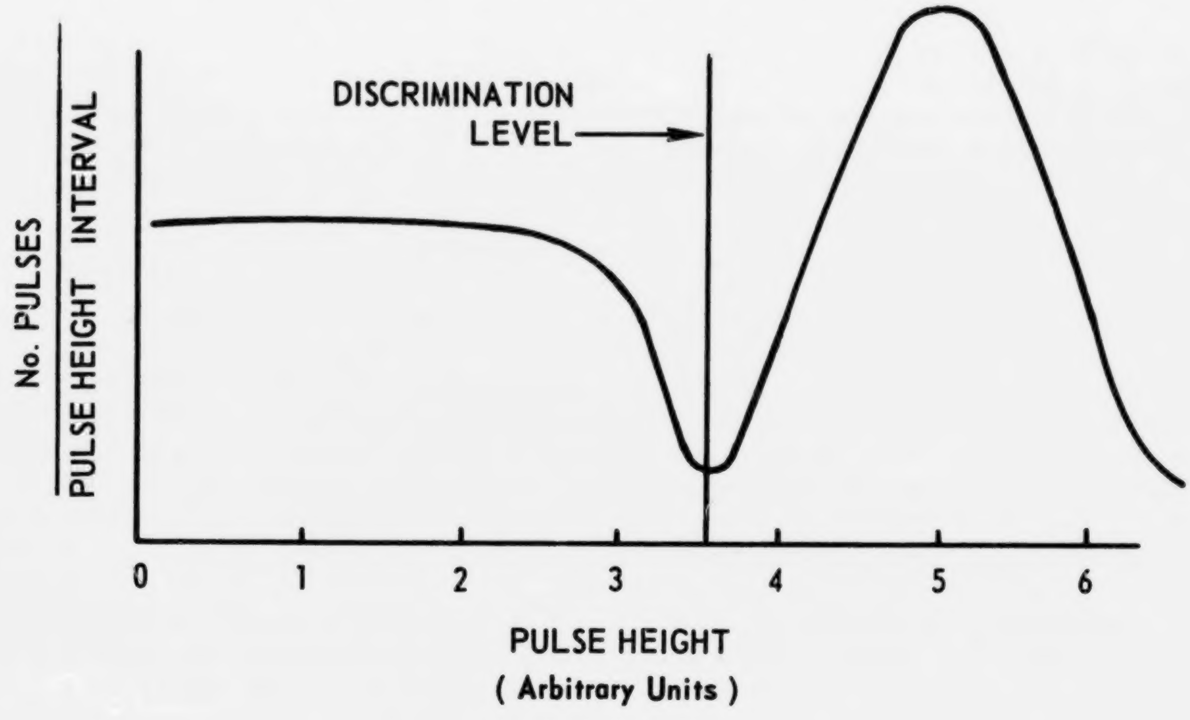

Figure VII-5.--Pulse Height
(Arbitrary Units)

F. Scaler-Timer

The scaler functions as an electronic adding machine, and it is commonly used with an attached mechanical register and timer. Each pulse passed by the discriminator causes a count to be recorded by the scaler. Scalers may be designed with either binary or decade systems. The binary system employs a "scale of two" and has a number of selective scaling factors--usually 8, 16, 32, 64, 128, 256, and 512--with neon interpolation lights.

The total count is obtained by multiplying the register reading by the appropriate scaling factor and adding the sum count indicated by the interpolation lights. The decade system uses four "scales of two" that are electronically connected in such a fashion that for every ten input pulses, one output pulse is registered. Counts registered by the decade system can be read directly.

The register used with scaling circuits consists of either a relay-operated mechanical register or a recording device which indicates the number of pulses received from the last scaling stage.

Most scalers employ a timer which will automatically stop the scaler from counting at the end of a preset time. Many have the added capability of automatically stopping the count when a preset number of counts have been recorded. Whether one uses a preset time or a preset count depends upon factors peculiar to the application of interest.

III. INTEGRAL SYSTEMS FOR ALPHA AND BETA COUNTING

The block diagram of a typical alpha or beta counter would look the same as the one for a gamma scintillation counter (see Figure VII-1) except for the detector assembly. Also, the associated electronics perform the same functions with one notable exception: the discriminator is used primarily to eliminate thermal noise pulses and to discriminate against radiations which have different specific ionization properties.

A. End-Window Geiger-Mueller Counter

This instrument, primarily designed for the counting of beta radiation, is also sensitive to gamma rays, although its gamma efficiency is very low compared to sodium iodide crystals. The instrument is capable of detecting alpha particles if their energy is not totally absorbed by the air space between the sample and the detector and/or by the detector window itself.

1. Detector construction

The end-window Geiger-Mueller detector as used in laboratory counting systems is usually a cylindrical glass tube with a plastic base on one end. (See Figure VII-6.) A plastic rim on the other end of the tube holds a thin mica window of 1 to 3 mg/cm^2 thickness in place. The tube is filled with helium or argon and a quenching gas, such as alcohol vapor or a halogen gas. The central electrode (cathode) consists of a thin wire about .01 inches in diameter. The outer electrode (cathode) consists of a layer of copper or silver plating on the glass wall of the tube.

2. Detector operation and shielding

Each end-window G-M tube has its own characteristic curve. This curve is established by placing a source opposite the tube window; if the counter voltage is then increased in 25 to 50 volt steps, with counting rates being established for each voltage setting, a characteristic curve

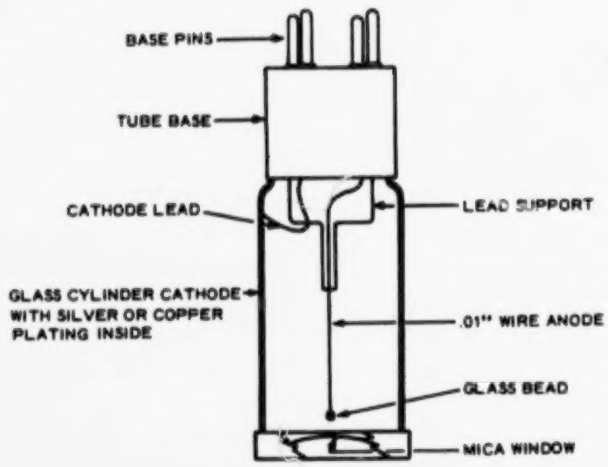
BASE PINS
TUBE BASE
CATHODE LEAD
LEAD SUPPORT
GLASS CYLINDER CATHODE WITH SILVER OR COPPER PLATING INSIDE
.01" WIRE ANODE
GLASS BEAD
MICA WINDOW

Figure VII-6.--End-Window Geiger-Mueller Counter

may be plotted. The usual curve has a plateau section (see Figure VII-7) wherein the counting rate shows only a small change with voltage variations. The tube operating voltage is usually selected about $\frac{1}{3}$ the plateau length from the threshold to the breakdown voltage.

The G-M tube is normally placed in a brass-lined lead shield or "pig" in order to cut down the background count. A typical lead shield weighs several hundred pounds.

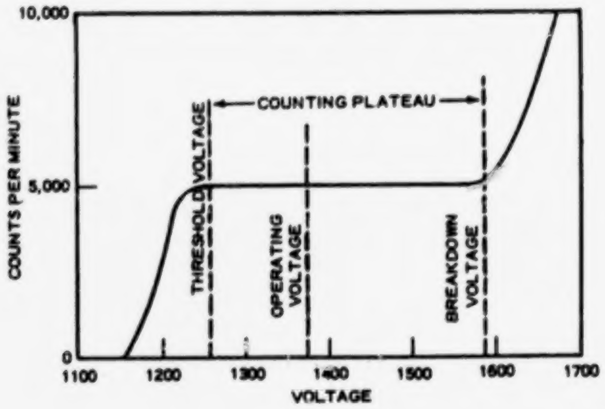

Figure VII-7.--Characteristic Curve of Typical G-M Tube

3. Associated electronics

The only difference between the associated electronics for the G-M tube and that for the gamma scintillation system previously described are due to differences in the size of the pulses produced in the detector.

The large pulses produced within the G-M tube need no preamplification. Therefore no preamplifier is generally employed with the G-M tube.

Since all pulses from the G-M tube are approximately of equal height, (i.e., the tube is saturated with ions on every event regardless of the energy of the ionizing particle) the discriminator serves to block small pulses due to electrical and thermal noise rather than eliminate part of the spectrum as with the gamma scintillation counter.

B. Proportional Counter

Proportional counters are designed to detect both alpha and beta particles. They may be constructed so that the sample is either inside or outside the sensitive volume of the detector. The former, called internal proportional counters, offer the advantage of increased efficiency because of the more favorable geometry arrangement. Their major disadvantage is that liquid samples cannot be counted inside the counting chamber owing to the quenching effect of water vapor. Also, they become contaminated easily from dry samples. The internal and external proportional counters exhibit similar operating characteristics. They differ only in construction; the external chamber having a very thin mica or mylar window similar to the end-window G-M tube. The internal counter is described here as a prototype of proportional counters.

1. Construction

The internal proportional counter detector is a chamber usually designed as a steel hemisphere. (See Figure VII-8.) The bottom of the chamber supports the sample dish and is called the piston. It is joined to the

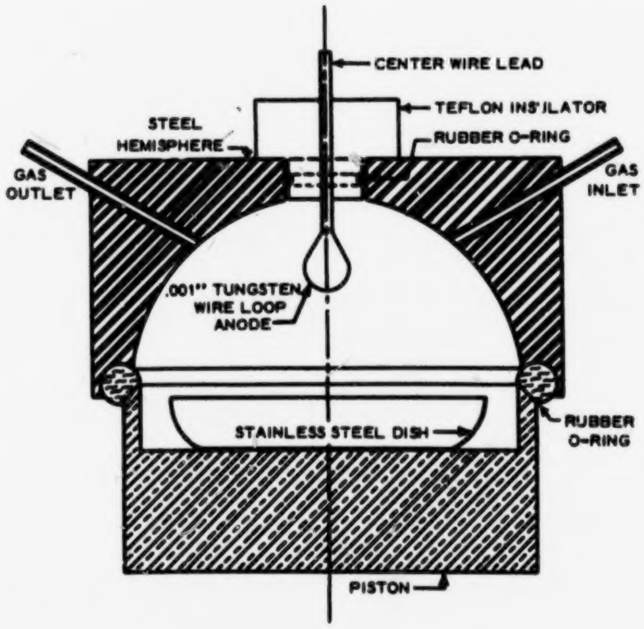

Figure VII-8.--Internal Proportional Counter Chamber

hemisphere (when counting) at a rubber O-ring junction. A plastic insulator holding a tungsten wire loop anode 0.001 inches in diameter is inserted in the top of the hemisphere. The hemisphere wall functions as the cathode and contains a counting gas inlet and outlet. Since the water molecules in atmospheric air have an affinity for electrons, the pressure of air in the chamber will diminish or "poison" an alpha or beta count. Hence, the chamber is purged with a counting gas mixture (usually 90% argon and 10% methane) before a count is made to remove all air molecules. This same gas flows through the chamber during a counting period so that a positive pressure inside the chamber will insure against air leaks at the O-ring seal.

2. Operation

The internal proportional detector exhibits a characteristic curve with 2 plateaus, each similar to that for the G-M tube. (See Figure VII-9.)

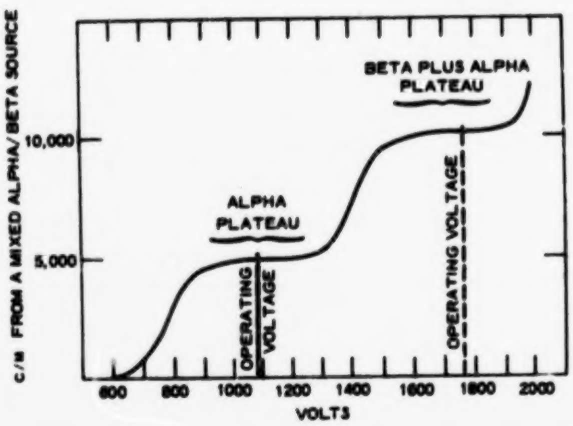

Figure VII-9.--Operating Curve for a Proportional Counter

The first plateau called the alpha plateau, has a typical voltage range of approximately 900 volts to 1,300 volts. The second plateau, called the beta plateau, typically has a voltage range of approximately 1,600 volts to 2,000 volts. The midpoint of each plateau is normally selected as the operating voltage. When the instrument is adjusted at the alpha operating voltage, only alpha particles are counted. When the instrument is adjusted at the beta operating voltage, both alpha and beta particles are counted. In order to count only beta particles, the chamber may be operated on the beta plateau with an aluminum foil of about 8 mg/cm^2 thickness placed on top of the sample to shield out the alpha particles. Of course, an indeterminate fraction of the lower energy beta particles will also be stopped in this shield. An equally precise and somewhat more convenient procedure is simply to count the alphas on the alpha plateau, the alphas and betas on the beta plateau, and subtract in order to obtain the net beta count. (This method would be exact, except for the alpha plateau slope of a few per cent per hundred volts, which causes each alpha to produce about 1.1 to 1.2 counts on the beta plateau. In practice, this slope is easily measured and an exact correction to the data may be made.)

3. Counter circuitry

A preamplifier, amplifier, and a discriminator characterize the typical prescaling circuitry in an internal proportional counter. The linearity requirements of amplifiers used with both proportional and scintillation counters are greater than for G-M counters. At the alpha operating voltage, the discriminator makes possible selective response to alpha particles with little or no response to high intensities of beta and gamma radiation. An alpha particle may produce a total of 10^8 primary and secondary ionizations in the chamber while a single beta particle or gamma ray may produce a total of 10^5 ion pairs. If the discriminator is adjusted to respond only to a minimum of 10^8 ionizations for each initial ionizing event, a count of only alpha particles will be recorded.

C. Solid Scintillation Counters for Alpha and Beta Counting

Counting systems utilizing solid scintillation media for alpha and beta counting do not differ from gamma scintillation systems in construction and operation -- only the detection media differ. As mentioned in Chapter VIII, a thin layer of silver-activated zinc sulfide is used to detect alpha particles, and anthracene or some plastic scintillator may be used as a beta detector.

D. Liquid Scintillation Counters for Beta Particles

Liquid scintillation counters have become very important in recent years for counting low energy beta emitters such as ^{14}C and ^{3}H. However, liquid scintillation detectors are seldom used in integral counting systems. The counting system is rather complex, and is discussed in Chapter VIII.

V. SUMMARY

Integral laboratory systems are those that count all pulses larger than a certain size. A single discriminator is used to electronically block out small pulses. Scintillation media, G-M tubes, and proportional chambers are used as detectors in these systems. With few exceptions, the associated electronics are very similar for all integral counting systems.

SUGGESTIONS FOR FURTHER READING

1. Wagner, H.N., Principles of Nuclear Medicine, W.B. Saunders Co. (1968), pp. 149-160.

2. Blahd, W.H., Nuclear Medicine, McGraw-Hill Book Co. (1965), pp. 80-86.

3. Quimby, E.H. and Feitelberg, S., Radioactive Isotopes in Medicine and Biology, Lea and Febiger, Vol. 1 (1965), chap. 13.

CHAPTER VIII

LABORATORY COUNTING SYSTEMS
II. Pulse Height Analyzers

I. INTRODUCTION

Often, the accuracy of a procedure is enhanced by "window" counting rather than integral counting; i.e., only a portion of a gamma spectrum such as the one described in Chapter VII is counted. This necessitates both lower and upper discrimination levels. Further instrumentation refinements enable one to sort pulses in such a way that an entire spectrum can be viewed at one time. This technique is termed *spectroscopy*.

Several of the different types of detection media discussed in Chapters VI and VII can be used in conjunction with a pulse height analyzer. However, scintillation detectors are, by far, the most common ones used in such systems. In nuclear medicine laboratories, pulse height analyzers are used primarily in gamma counting systems using NaI(Tl) detectors, and in liquid scintillation systems for beta counting.

II. GAMMA COUNTING SYSTEMS USING PULSE HEIGHT ANALYZERS

A block diagram of a typical gamma counting system utilizing a pulse height analyzer is given in Figure VIII-1. The detector assembly, pre amp, linear amplifier, and high voltage supply perform the same functions as described in Chapter VII. The pulse height analyzer, with which a variety of data readout devices may be employed, has replaced the discriminator section of the single channel analyzer.

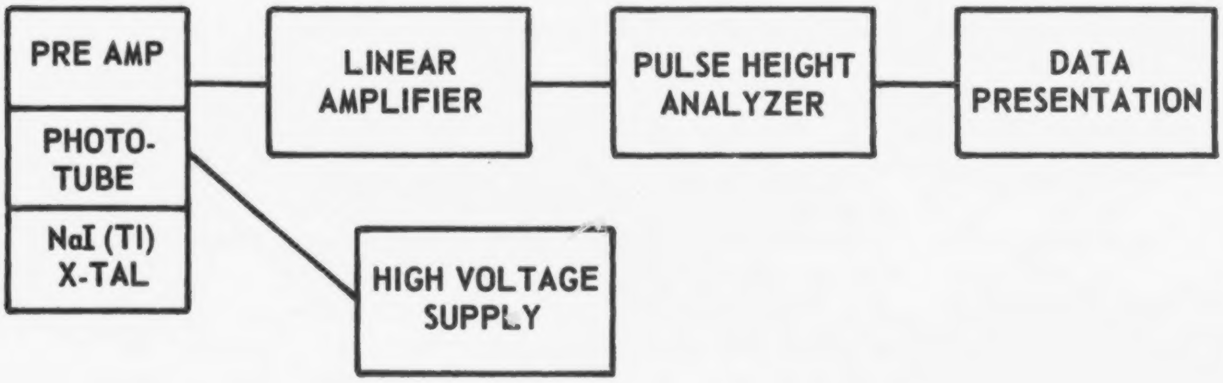

Figure VIII-1.--Block Diagram of a Pulse Height Analyzer System

A. Pulse Height Analyzers

Pulse height analyzers are of two types--voltage discriminator and computer.

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1. Voltage discriminator

a. Operation

Consider the gamma spectrum of ^{131}I (see Figure VIII-2) one of the most

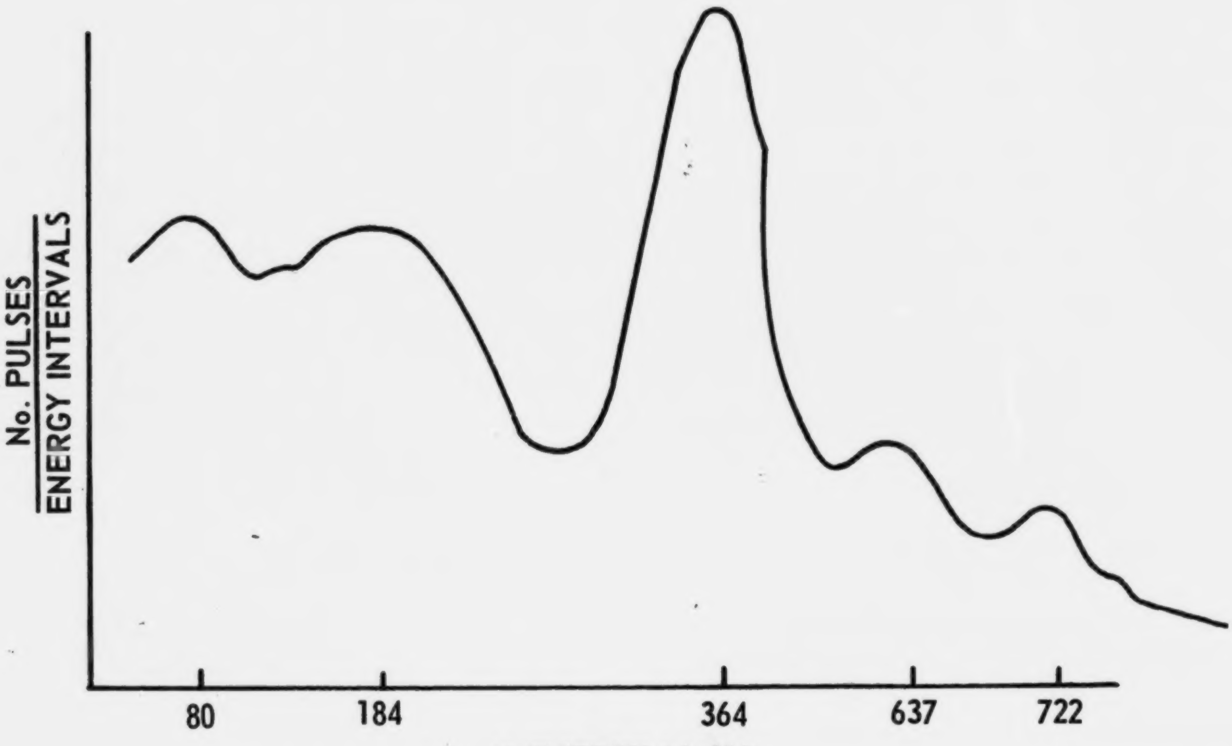

Figure VIII-2.--Gamma Spectrum of ^{131}I

widely used radioisotopes in nuclear medicine. Unlike the ^{137}Cs spectrum in the examples in Chaper VII, ^{131}I has a number of different gamma energies. The most abundant photons have 364 keV of energy. However, gammas with energies of 80 keV, 184 keV, 637 keV, and 722 keV are also emitted by ^{131}I. Hence, the gamma spectrum has several photopeaks. (Note: It is suggested that the student review the material in Chapter VII on gamma interactions and pulse height spectrum at this point.)

Sometimes it is advantageous to count only those pulses arising from total absorption of the 364 keV photon. This can be done by using two voltage discriminators in conjunction with an anticoincidence circuit, as shown in the block diagram in Figure VIII-3.

Pulses from the linear amplifier are sent simultaneously to lower and upper level discriminators. The discrimination levels are set at the lower and upper limits of the energy range to be counted. Pulses larger than the lower discrimination level are transmitted by the lower level discriminator, and similarly for pulses larger than the upper-discrimination level. It follows that all pulses transmitted by the

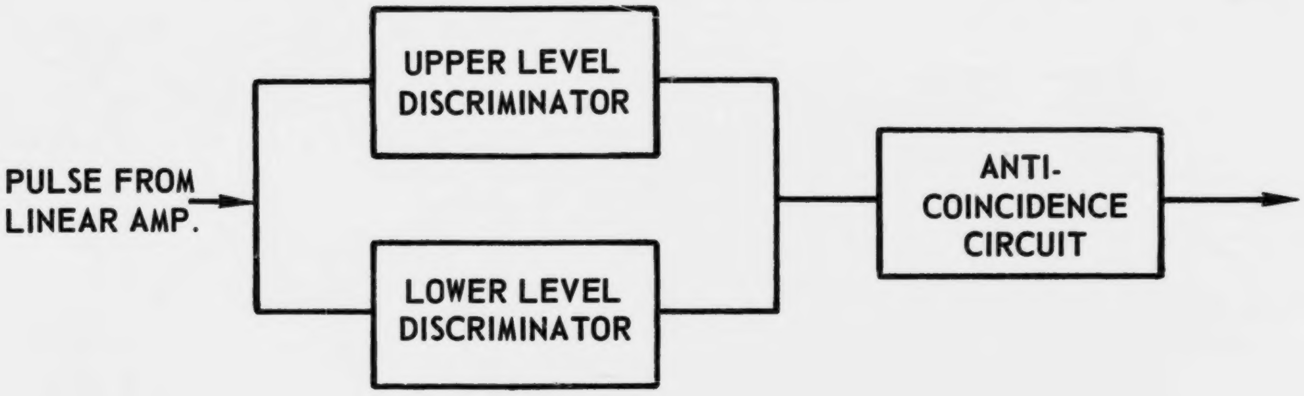

Figure VIII-3.--Block Diagram of a Voltage Discriminator Pulse Height Analyzer

upper level discriminator (U.L.D.) will also be passed by the lower level discriminator (L.L.D.). In other words, pulses arising from photons with energies below the range of interest are transmitted by neither discriminator, while those pulses representative of energies greater than this range are transmitted by both discriminators. Obviously, some means must be employed to transmit those pulses that trigger the L.L.D. but not the U.L.D.; i.e., pulses that fall between the two discrimination levels. This is done with an anticoincidence circuit which will transmit a pulse arriving at its input from the L.L.D. only if one does not arrive from the U.L.D. at the same time.

Figure VIII-4 diagrammatically describes the operation of the voltage discriminator pulse height analyzer. The first pulse from the linear amplifier (top of diagram) is too small to trigger even the L.L.D. (set at three pulse height units). Consequently, it is rejected by the analyzer. The second pulse triggers the L.L.D., but it also triggers the U.L.D. (set at four pulse height units). It too is rejected because the pulses from the L.L.D. and the U.L.D. arrive at the input of the anticoincidence circuit at the same time. The third pulse triggers the L.L.D., but not the U.L.D. Therefore, it is accepted by the analyzer and transmitted to the recording mechanism. The energy interval represented by the difference in the discrimination levels is called the "window width." All pulses falling within the window are counted.

The application to the ^{131}I example is illustrated in Figure VIII-5. The discrimination levels are set to include only those pulses arising from total absorption of the 364 keV gamma. Of course, some scatter from the two higher energy photons will be included in this energy range.

b. Calibration

Pulse height analyzers vary as to the controls available and their functions. However, the principle of calibration is the same for all. As mentioned in Chapter VII, the position of the photopeak (i.e., pulse height for a given amount of energy absorbed) is controlled in two ways:

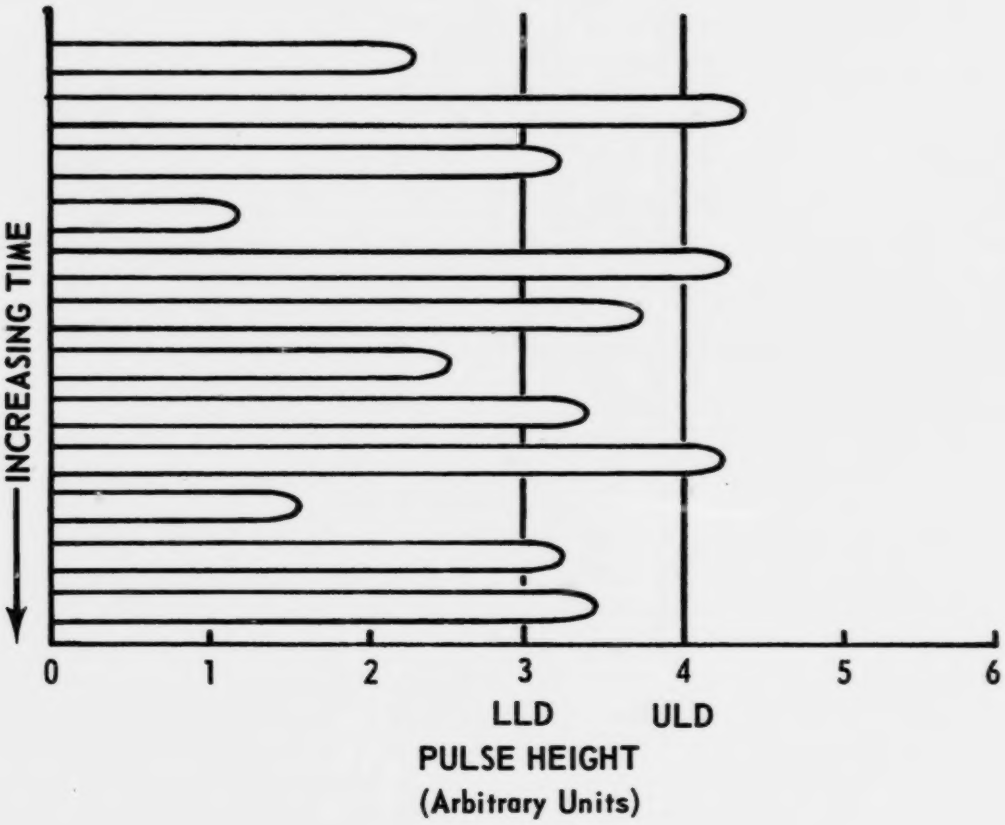

Figure VIII-4.--Pulse Height
(Arbitrary Units)

by varying the high voltage on the phototube, and by varying the gain on the linear amplifier. Pulse height per unit of energy absorbed is directly proportional to both these parameters. Many voltage discriminator analyzers have completely independent upper and lower level discriminator controls. Others have a lower level control (sometimes called base-line) and a window-width control coupled to the base line control. In either case, the energy scale is calibrated with a source of known gamma energy and, by means of the gain and high voltage controls, by moving the spectrum up and down until the photopeak of interest is centered in the chosen window. Each instrument has the proper calibration procedure outlined in the instruction manual. The instruction manual should be followed precisely in calibrating and operating any pulse height analyzer system.

c. Types

Voltage discriminator pulse height analyzers of the type described above are called single channel analyzers; i.e., only one set of discriminators is employed. Many counting systems have two or three sets of discriminators (two or three "channels"), and each channel has its own scaler or readout device. This permits simultaneous counting of more

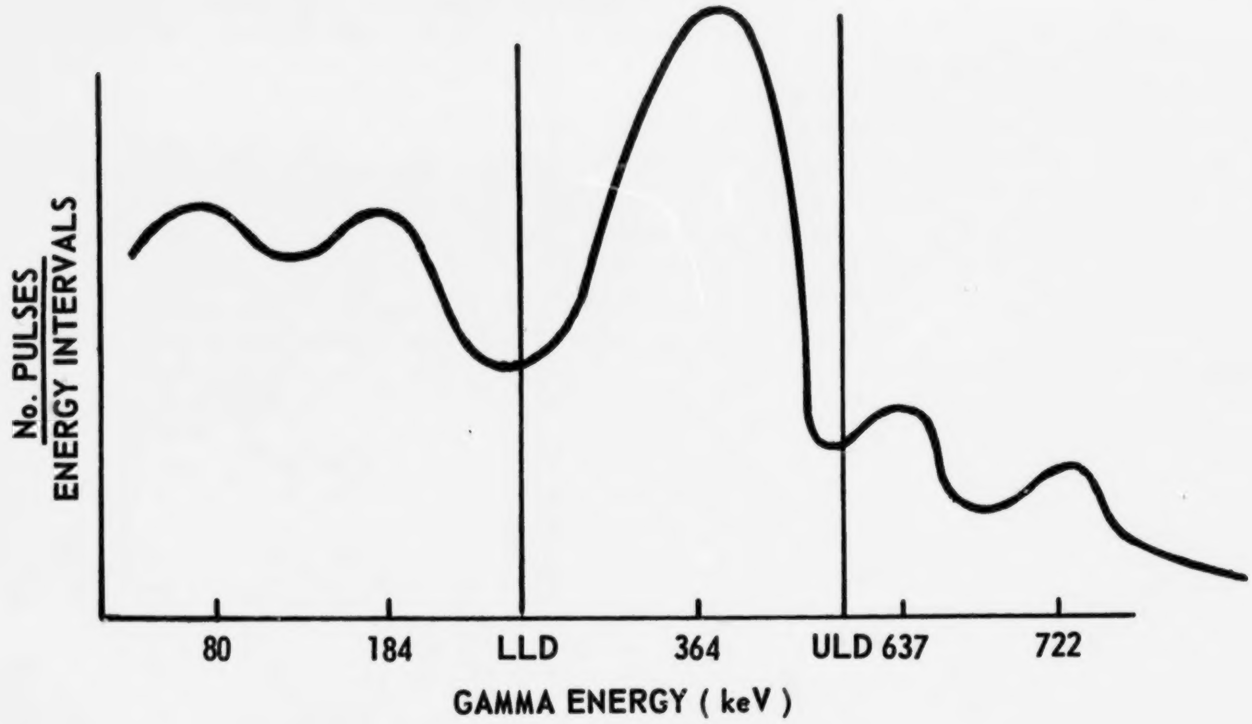

Figure VIII-5.--Gamma Energy (keV)

than one photopeak. Such instruments are employed to greatest advantage in counting samples that contain more than one radioisotope, e.g., simultaneous iron-59 and chromium-51 study.

An entire gamma spectrum may be obtained by using a single-channel analyzer with a very narrow window and moving the window one step at a time over the spectrum, counting at each position for equal times. Some instruments have automatic "scanning" mechanisms which automatically move the window over the entire spectrum. A permanent graph of the spectrum may be obtained by using the appropriate readout device.

2. Computer-type

a. Theory

Pulse height analyzers which incorporate certain aspects of computer circuitry are called computer-type or "multichannel" analyzers. Such instruments can sort and store information into as many as 4,096 separate channels.

The two main components of the computer-type analyzers are the analog-to-digital converter and the memory. The purpose of the analog-to-digital converter is to take the voltage signal from the linear amplifier and convert it to a number that is proportional to the size of the pulse. This is accomplished in most analyzers by converting the voltage signal to a time interval, which can be measured very precisely. The time interval is proportional to the pulse height. It determines the memory location into which the pulse will be stored. Thus, all pulses of the same size are stored in the same location. The number of possible memory locations is equal to the number of channels available in the instrument. So, the entire pulse height spectrum resulting from gamma interactions in the crystal is stored in a memory from which the information can be retrieved and displayed in various ways, depending on the type of readout device employed. Figure VIII-6 shows a ^{137}Cs gamma spectrum obtained on a Victoreen model 400-channel pulse height analyzer. The backscatter peak at 0.22 MeV is the result of photons from the source undergoing 180° Compton collisions in the shield.

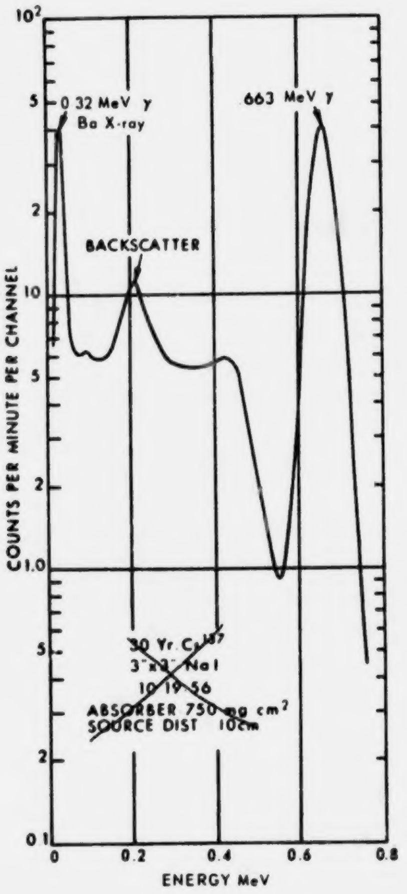

Figure VIII-6.--Spectrum of Cesium-137

b. Calibration

Multichannel pulse height analyzers are calibrated basically the same as voltage discriminator analyzers; i.e., a known gamma spectrum is moved up and down the scale by the amplifier gain and detector high voltage until the photopeak is centered in the proper channel. (In some systems there is an additional gain control on the analog-to-digital converter.) Multichannel analyzers have the advantage of permitting observation of the entire spectrum with an oscilloscope or other readout device. For example, suppose one wishes to calibrate a 200-channel system so that the entire 200 channels cover an energy interval of 0 to 2 MeV. A good radioisotope for calibration in this range is ^{137}Cs with its gamma energy of 0.662 MeV. Since 200 channels covers 2 MeV of energy, the energy per channel calibration factor is 2,000 keV ÷ 200 channels, or 10 keV/channel. Then, the proper channel for the 0.662 MeV ^{137}Cs gamma is determined by the relation:

$$\text{channel no.} = \frac{0.662 \text{ keV}}{10 \text{ keV/channel}} = 66.2.$$

For calibration purposes this would be rounded to channel number 66, since one cannot read fractions of a channel directly. Once the desired channel number is determined, the gain and high-voltage controls are adjusted to make the photopeak fall in the desired channel. Normally, one would calibrate with more than one isotope to check the linearity of the system. For the conditions stated (0 to 2 MeV over 200 channels), ^{60}Co with gamma energies of 1.17 MeV + 1.33 MeV is a good isotope for checking linearity. No amplifier is perfectly linear over its entire range. Thus, a calibration factor determined with a high energy gamma photon (>1 MeV) should not be used for low energy photons (<300 keV). One should always calibrate the pulse height analyzer with standard sources which emit photons in the energy range of interest.

B. Data Presentation

Several types of readout devices are available for use with pulse height analyzer systems. They may be divided into two categories, analog and digital.

In digital data presentation systems, a number or some other coded character is generated for each pulse reaching the input of the readout device. Examples of digital systems are scalers, electric typewriters, parallel printers, paper punch tape, and magnetic recording tape.

In most analog data presentation systems, a voltage signal is generated. This signal is proportional in height to either the number of counts in a channel or the rate at which counts are being received by the readout device. Examples of analog systems are ratemeters, strip-chart recorders, oscilloscopes and X-Y plotters.

1. Analog readout devices

a. Ratemeter

In a ratemeter, the individual pulses from the discriminators are averaged by means of an "RC" circuit, and a voltage signal proportional to the average rate at which counts are coming in is measured by means of a voltmeter. A very important parameter associated with the ratemeter is the "RC constant" or "time constant." The time constant is the product of the resistance (in ohms) and the capacitance (in farads) in the input circuit of the ratemeter. The time constant refers to the time required for the ratemeter to respond to a sudden change in counting rate. One time constant is the time required to respond to the change by an amount equal to 63% of the difference between the old and new counting rates. Two time constants result in 86.5% of the total change, three time constants 95% and so on. In general, several[1] time constants are required for the change to reach a value arbitrarily close to the new steady-state reading. For example, Figure VIII-7 illustrates the use of a ratemeter with a time constant of five seconds. The initial steady-state counting rate is 2,000 cpm.

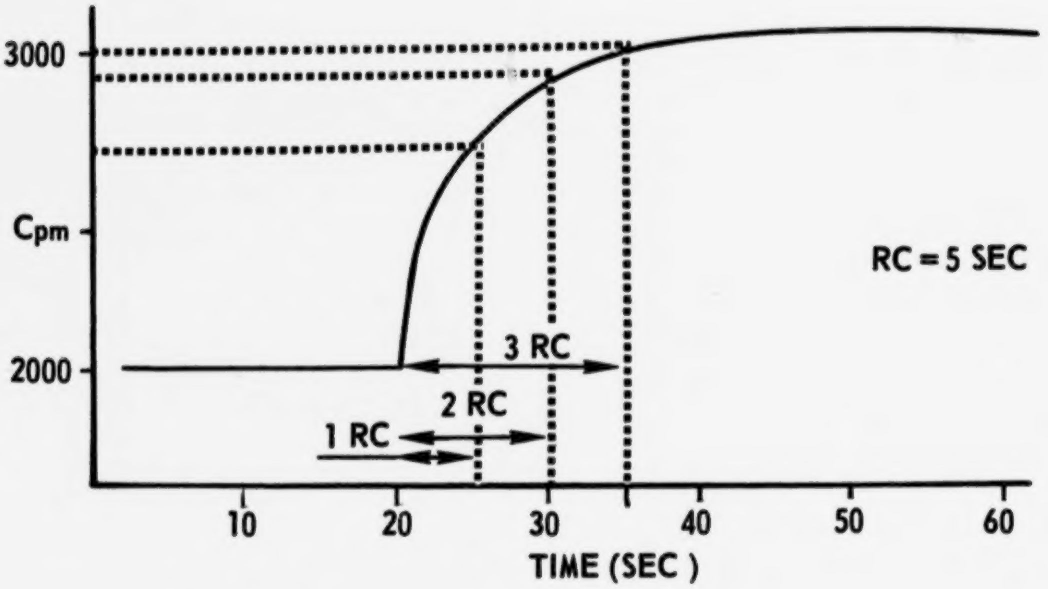

Figure VIII-7.--Exponential Response of an Analog Ratemeter

At $t = 20$ seconds, the counting rate suddenly jumps to 3,000 cpm. The ratemeter, however, has not fully responded to this change in counting rate until 25 to 30 seconds have elapsed ($t \approx 45$ seconds).

b. Strip chart recorder

A strip chart recorder produces an inked paper recording of counting rate as a function of time. The paper travels at a constant speed, variable from about one inch per hour to about eight inches per minute. An ink stylus marks the paper. (See Figure VIII-8.) The strip chart recorder

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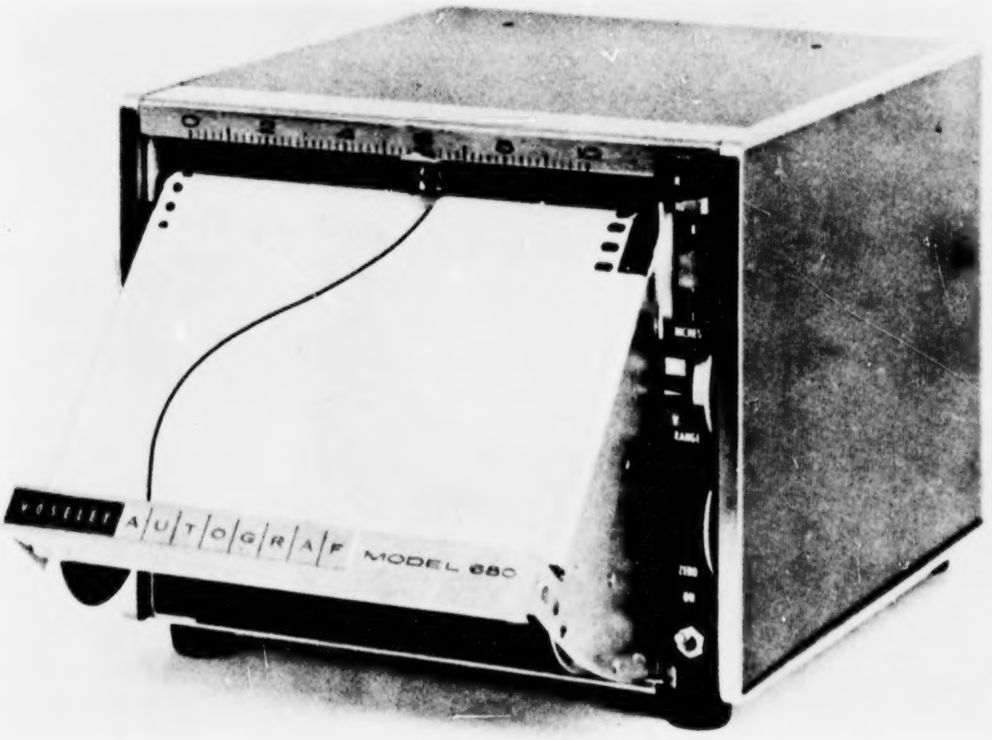
[1] The number of time constants required for the meter reading to come within, say, one standard deviation of the new steady-state value depends on the magnitudes of the counting rates. A rule of thumb is that 5 time constants are generally sufficient.



NOT REPRODUCIBLE

Figure VIII-8.--Strip Chart Recorder
(Courtesy of Hewlett-Packard/Mosley Div.)

is used primarily in conjunction with a ratemeter single-channel analyzer combination. The counting rate signal from the ratemeter drives the strip chart recorder, providing a permanent record of the counting rate vs. time. Such systems find their greatest clinical application in dynamic function studies, since the time factor is of the utmost importance in physiologic processes.

c. Oscilloscope

The oscilloscope is used in multichannel analyzer systems with computer-type pulse height analyzers. It provides an immediate, visible, non-permanent, graphic representation of the counting rate per channel vs. channel number. (See Figure VIII-9.) The oscilloscope consists basically of a cathode ray tube with vertical and horizontal deflection plates to focus the electron stream at the proper position on the phosphorescent face of the tube each time a count is recorded.

Advantages of having an oscilloscope on a multichannel analyzer are:

1. Growth of the graph indicates the counting rate. From this, a logical counting time may be set.

2. The oscilloscope provides a quick look at the spectra to determine if any malfunctions have occurred, e.g., channels dropped or shifted.

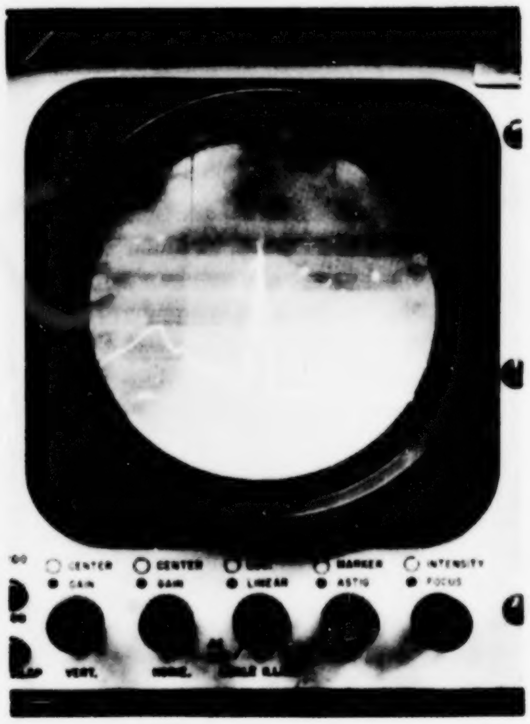


Figure VIII-9.--^{137}Cs Spectrum as Viewed on an Oscilloscope

3. It is very useful in the calibration of the gain settings of the instrument.

d. X - Y Plotter

The X-Y plotter is simply an automatic graph plotter. Like the oscilloscope, it is used mainly with multichannel analyzer systems. Once a gamma spectrum is stored in the memory of the analyzer, it can be retrieved and plotted on either linear or log paper by the X-Y plotter. It is much faster and more convenient than hand plotting a spectrum from the digital data, but less accurate.

C. Digital Readout Devices

1. Electric typewriter

An electric typewriter can type out accumulated information from a multichannel analyzer onto standard sized paper.

As with all digital readout devices, the exact number of counts per channel is recorded. The advantages of an electric typewriter include the ability to manually type pertinent information on the data sheet, and the ability to make several carbon copies.

2. Parallel printer

The parallel printer is also used with multichannel analyzer systems.

Whereas, the electric typewriter types one character at a time across the page, the parallel printer prints an entire line at once on a narrow strip of paper. Each line gives the channel number and the number of counts in that channel. (See Figure VIII-10.) The advantage of the parallel printer over the electric typewriter is increased speed. However, the printer cannot type in pertinent information nor make carbon copies.

```
006    00549
005    00691
004    00474
003    00106
002    00067
001    00000
```

Figure VIII-10.--Parallel Printer Tape Format

3. Paper punch tape

Paper punch tape is a roll of paper about 1 inch wide in which holes are punched according to a coded system, as shown in Figure VIII-11. These units offer versatility in that information may be read into the analyzer as well as punched out if a paper tape reader is also employed. Also, data punched onto paper tape may be processed directly by a properly programmed digital computer.

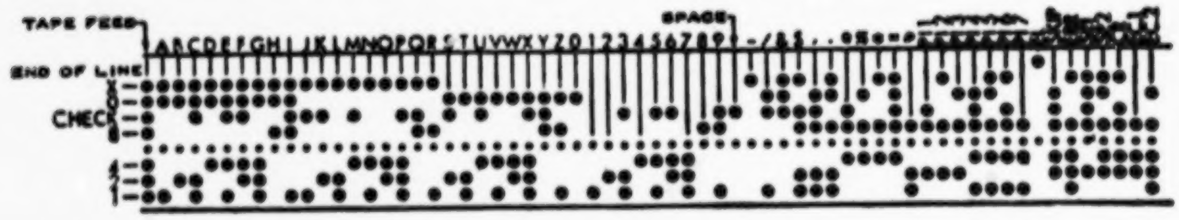


Figure VIII-11.--Paper Punch Tape - Eight Channel Code

4. Magnetic tape

Magnetic tape units are very similar in operation to paper punch units. However, instead of punched holes in the tape, small spots or bits along the length of the tape are magnetized according to some code, as illustrated in Figure VIII-12. Magnetic tape is much faster than paper tape, and can thus handle larger volumes of data. However, magnetic tape units are much more expensive.

5. Scalers

Scalers are discussed in Chapter VII in conjunction with integral counting systems. They are also used with voltage discriminator analyzers,

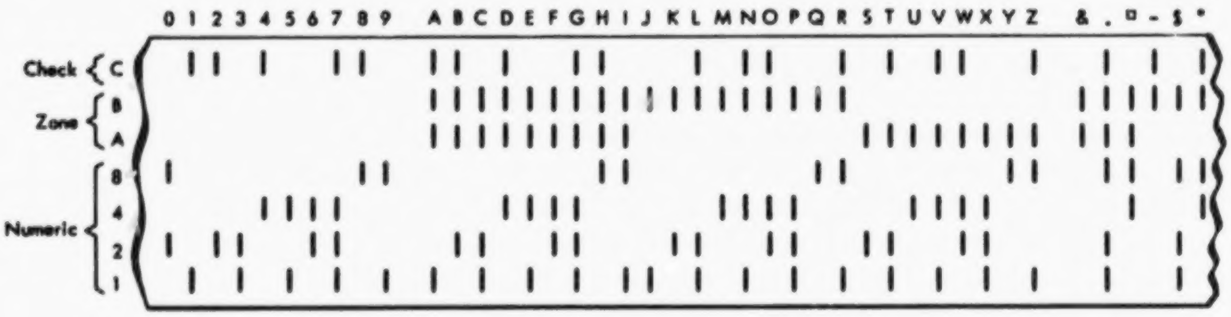

0 1 2 3 4 5 6 7 8 9 A B C D E F G H I J K L M N O P Q R S T U V W X Y Z & . ¤ - $ *
Check
C
Zone
B
A
Numeric
8
4
2
1

Figure VIII-12.--Magnetic Tape - Seven Bit Code

but the fact that they must be read manually precludes their use with computer-type multichannel analyzers on a routine basis.

III. LIQUID SCINTILLATION COUNTING SYSTEMS

Liquid scintillation counters are used primarily for counting emissions from low energy beta emitters such as ^{14}C and ^{3}H. These materials are troublesome to count with most detectors because of their low beta energy (156 keV for ^{14}C and 18.6 keV for ^{3}H). Liquid scintillation detectors offer the advantage of having the sample intimately mixed with the scintillation medium. One problem still persists, however: Thermal emission of electrons from the cathode of a photomultiplier tube cause the background in a single phototube system to fluctuate and prohibit counting of low levels of these isotopes, even at low temperatures. Thus, in addition to placing the sample, scintillator, phototube, and preamp in a commercial freezer, a dual phototube preamp arrangement with coincidence and logic circuits as shown in Figure VIII-13 is employed.

In this system, scintillations from the beta particles are seen by two phototubes. The resulting pulses are shaped and amplified and appear simultaneously at the inputs of the monitor and analyzer amplifiers. If the output pulse from the monitor exceeds the discrimination level of discriminator C, a signal passes through the coincidence circuit and opens a gate in the logic circuit for a given duration. During this period a pulse occurring in the analyzer phototube which exceeds the setting of discriminator A but not discriminator B will pass through the logic to the scaler and be counted. Pulses smaller than the discrimination level of A will not be passed; those that exceed the level of B will be killed in logic. Hence, pulses are counted only if they arise in both phototubes simultaneously. Since thermal noise pulses produced in the analyzer phototube would not ordinarily occur simultaneously in the monitor phototube, they are killed in logic even though they may be of the proper height to pass the discriminators.

Some liquid scintillation counting systems have the analyzer detector output divided into two or three separate counting channels. The discrimination levels are independently adjustable for each channel. Each channel has its own logic circuit and scaler.

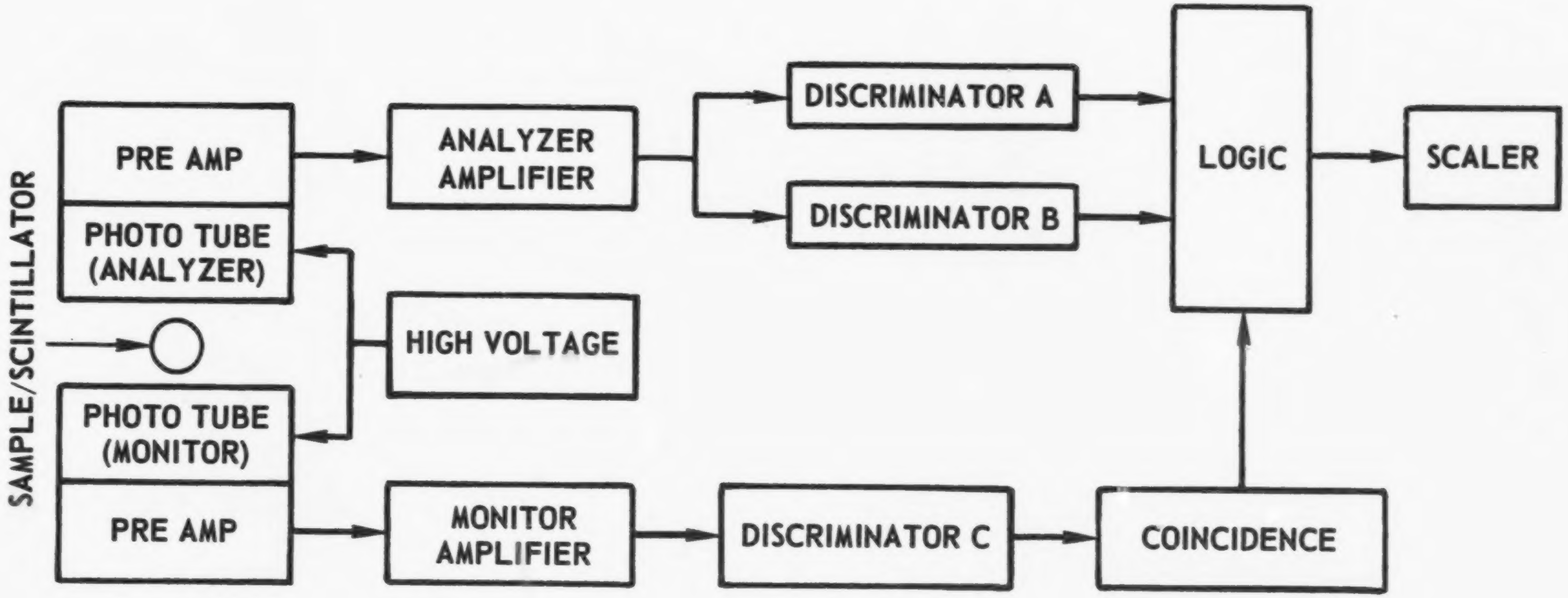

SAMPLE/SCINTILLATOR
PRE AMP
PHOTO TUBE (ANALYZER)
PHOTO TUBE (MONITOR)
PRE AMP
ANALYZER AMPLIFIER
HIGH VOLTAGE
MONITOR AMPLIFIER
DISCRIMINATOR A
DISCRIMINATOR B
DISCRIMINATOR C
LOGIC
COINCIDENCE
SCALER

Figure VIII-13.--Simplified Block Diagram of a Single Channel Liquid Scintillation Counting System

Suggestions for Further Reading

1. Wagner, H.N., Principles of Nuclear Medicine, W.B. Saunders Co. (1968), pp. 138-149 and 160-163.

CHAPTER IX

MEDICAL RADIOISOTOPE SCANNING INSTRUMENTATION

I. INTRODUCTION

The use of radiation detecting instruments to visualize the distribution of a radioactive material in an organ or gland is called scanning. Instruments of this type developed in the early 1950's were used primarily to scan the thyroid gland. By 1956, however, successful scans of the liver, brain, and many other sites had been achieved. Today scanning is widely accepted as a valuable diagnostic tool.

Scanning instrumentation has undergone much improvement in the last several years and some highly sophisticated devices are now available. Two basic types of instruments have emerged--"rectilinear" scanners and "stationary imaging" devices.

II. RECTILINEAR SCANNERS

The major components of most commercially available rectilinear scanners are diagrammed in Figure IX-1.

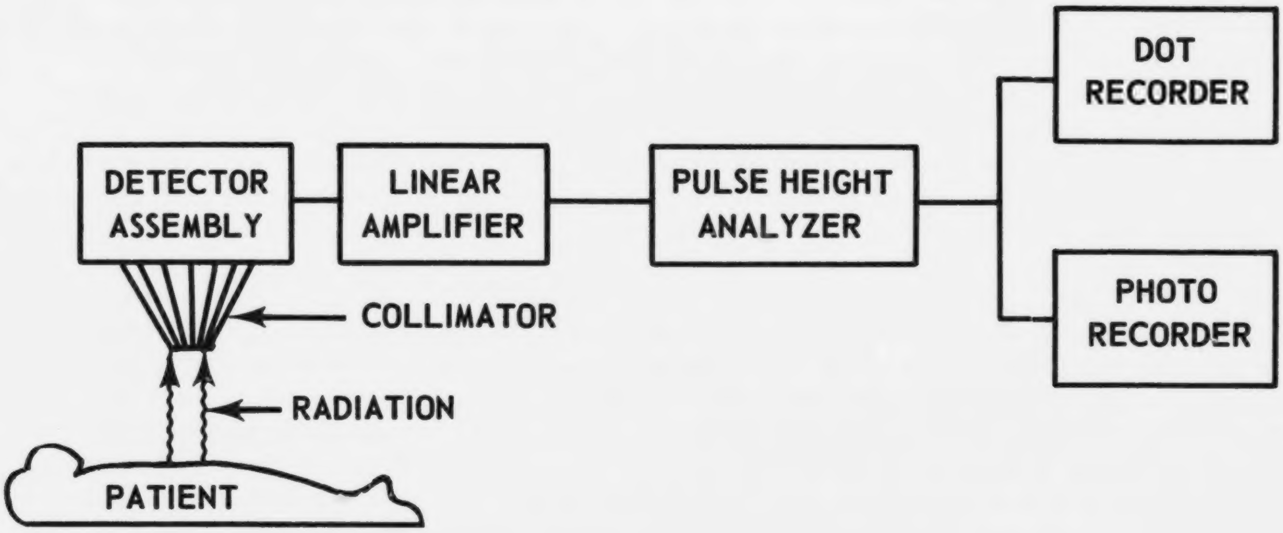


Figure IX-1.--Simplified Block Diagram of a Typical Rectilinear Scanner

As the detector-collimator assembly moves back-and-forth across the area of interest, gamma rays from the patient interact within the NaI detector producing an electrical signal at the output of a photomultiplier tube which is optically coupled to the detector. The signal is amplified and, if it is the proper size, is transmitted by the pulse height analyzer to the scan recording mechanisms. The recording apparatus is mechanically or electronically coupled to the detector assembly so that a 1:1 correspondence exists between the movement of the detector assembly and that of the recording mechanisms. For each signal transmitted by the pulse height analyzer a mark is recorded on paper by a tapper or an electronic stylus. At the same time, a light source is energized momentarily which exposes a small spot on a sheet of photographic film. The paper recording is commonly referred to as a "dot" scan; the photographic representation is called a "photoscan." In the case of the dot scan, the ratio of recorded marks to incoming signals may be decreased by an appropriate factor to accommodate high count rates. In both types of scan recordings, the end result is a map of the distribution of radioactivity within the patient.

Of the components that make up the rectilinear scanning system only the detector-collimator arrangement and the scan recording mechanisms are unique to this particular instrument. The associated electronics (i.e., photomultiplier tube, preamp, linear amplifier, and pulse height analyzer) are common to gamma spectroscopy systems in general, and these are discussed in Chapter VIII. Only those components unique to scanning are discussed here.

A. Detector-Collimator Assembly

The purpose of the collimator is to limit the field of view of the detector to a relatively small volume of tissue. Collimators are usually constructed of lead, although tungsten and gold have been used experimentally. The collimator design, along with the diameter and thickness of the NaI crystal, largely determines the sensitivity and resolution of the scanning system. For purposes of this discussion, collimator resolution may be defined as the inverse of the diameter of the volume of tissue the detector "sees" at any given time. Sensitivity is defined here simply as a parameter inversely proportional to the time required to obtain a scan.[1]

Sensitivity and resolution are not independent parameters. They are related in such a way that, with few exceptions, a change in collimator design to improve resolution will be accompanied by a decrease in sensitivity. The following example will illustrate the point. Suppose a 3-inch-diameter crystal is to be used to scan an organ which is suspected of containing a lesion 2 cm in diameter. Figure IX-2 shows two sets of conditions which illustrate the interdependence of sensitivity and resolution. In Figure IX-2(a) a "straight bore" collimator with a hole diameter of 3 inches is used so that the entire crystal face is exposed to the radiation field at all times.

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[1] The terms "resolution" and "sensitivity," as they apply to the overall scanning system, have received close sematic scrutiny. Attempts have been made to define them in terms of strict physical parameters. A detailed discussion of this work is beyond the scope of this manual. The definitions stated above are sufficient for a qualitative understanding of collimator characteristics.

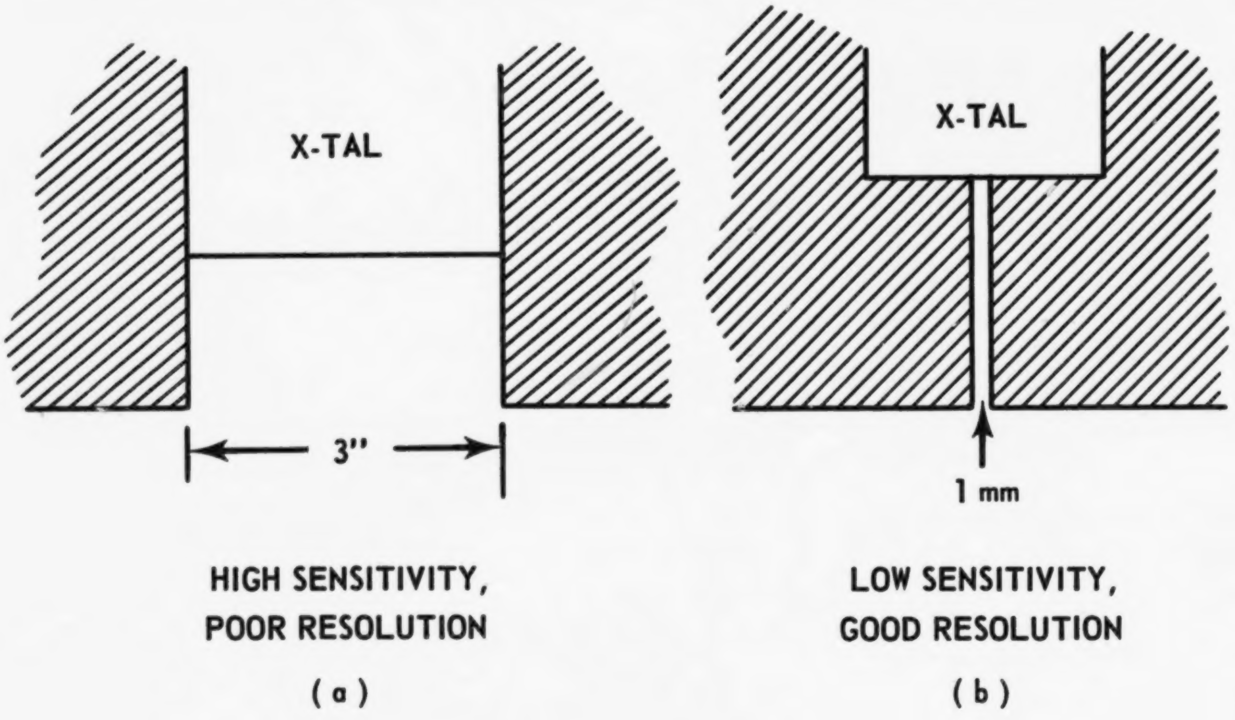
X-TAL
3"
HIGH SENSITIVITY, POOR RESOLUTION
(a)
X-TAL
1 mm
LOW SENSITIVITY, GOOD RESOLUTION
(b)

Figure IX-2.--Effect of Bore Size

Thus, as the detector moves over the organ, it responds to radiation from a volume of tissue at least 3 inches in diameter, and the likelihood of detecting a change in response due to a lesion 2 cm in diameter is nil. The resolution then is very poor but the sensitivity is very high because of the large volume of tissue to which the crystal is exposed. Figure IX-2(b) shows the opposite extreme in which all but a very small fraction of the crystal area is covered by the collimator. This arrangement would easily resolve a 2 cm diameter lesion provided the sensitivity was not reduced to the point that statistically significant differences in counting rate would be impossible to obtain in a reasonable period of time. Thus, a compromise must be reached between sensitivity and resolution. This has been best achieved to date by the focusing collimator which is described in the next section.

1. Collimator design

Factors peculiar to collimator design which affect sensitivity and resolution are: type of collimator, geometry, and transmission.

a. Type of collimator

Most present-day rectilinear scanners utilize a "focusing" type collimator, i.e., all of the holes focus to a point approximately 3 inches below the face of the collimator (illustrated in two dimensions in Figure IX-3). The plane to which the holes focus is called the focal plane of the collimator. The distance from the face of the collimator to the focal plane

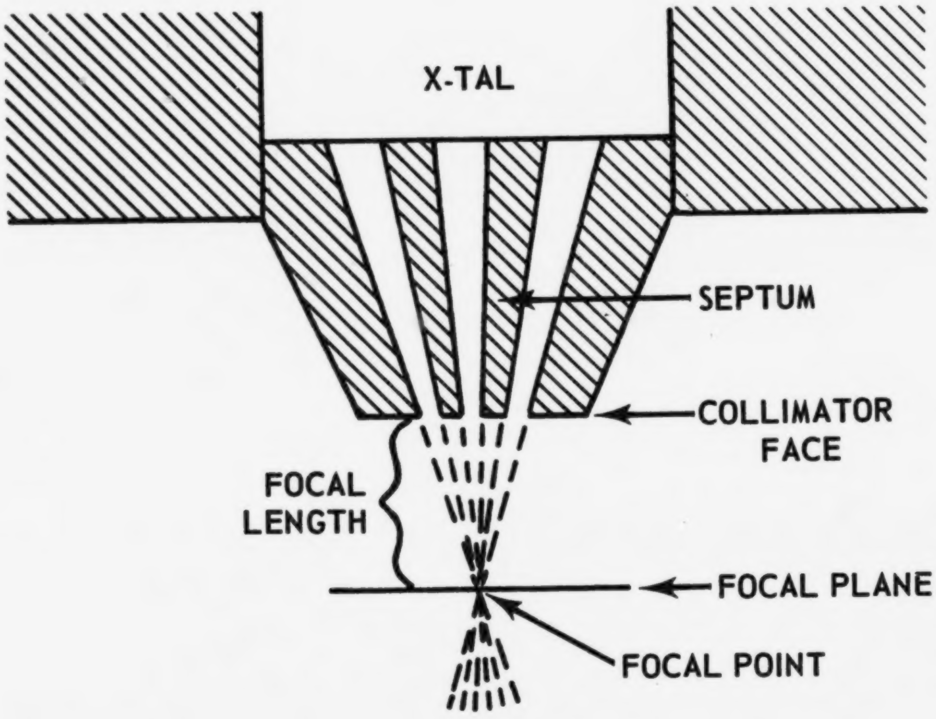

Figure IX-3.--Cross-section of a Focusing Collimator

is called the focal length. The focal point is the point of maximum sensitivity of the instrument, i.e., if a point source of a gamma-emitting radioisotope is moved about in front of the face of the collimator, the counting rate recorded by the instrument will be highest when the source is at the focal point. If the above procedure is carried out, and the observed counting rates at many points are recorded and mapped, a series of lines may be drawn connecting points of equal counting rate. This is referred to as an isoresponse curve and is illustrated in Figure IX-4 for two focusing collimators with different numbers of holes. The numbers in Figure IX-4 give the response at the outer edge of the area defined by each line as a percentage of the maximum response. It is noted that maximum sensitivity and resolution are at the focal plane. In fact, the "resolution distance" is sometimes defined as the width of the 50% isoresponse line measured at the focal plane.

b. Geometry

Geometry is defined as the solid angle around a point source subtended by the face of the sensitive volume of a detector. It is approximately equal to the ratio of the area of the face of the detector to the surface area of a sphere. The sphere has a radius equal to the distance from the point source to the face of the detector. Obviously, the greater the geometry the greater the sensitivity of the counting arrangement.

In focusing collimators, the geometry is determined by the diameter of the crystal and the distance from the crystal to the focal plane. The geometry is directly proportional to the diameter of the crystal and inversely proportional to the crystal-to-focal-plane distance. Stated another way, for a given maximum diameter of holes and a given focal length, the longer the collimator the better the resolution and the lower the sensitivity.

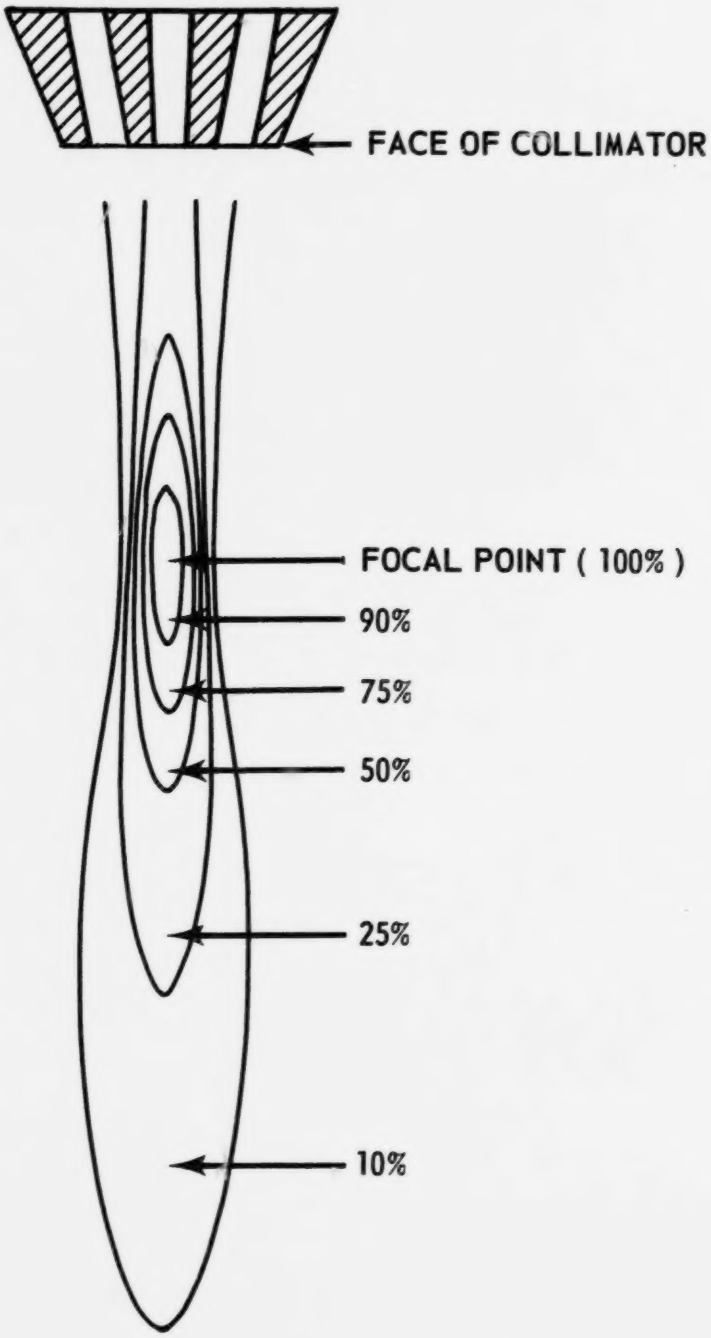

Figure IX-4.--Isoresponse Lines for a 37-Hole, 3 Inch Diameter Focusing Collimator

c. Transmission

Transmission is the fraction of the crystal face not obscured by the collimator when viewed from the focal point. For most collimators the transmission is 40% to 60%. The transmission is usually fixed; then the number of holes may be used to control the resolution of the collimator. For a given transmission, the more holes the better the resolution and the less the sensitivity. The holes are arranged hexagonally to provide the maximum number of holes in a given space. Six circles of equal diameter can be circumscribed about a circle of that same diameter. The minimum distance between the circumferences (septum thickness) will be the same for any two adjacent holes. Each additional ring of circles contains six more circles than the previous ring. Hence, collimators of 19, 37, and 61 holes have emerged. Hexagonal holes result in a considerable increase in transmission, compared to circular holes, without affecting the minimum septum thickness. The optimum septum thickness depends upon the gamma-ray energy of the isotope of interest. The septa must be of sufficient thickness to prevent significant penetration by the radiation.

Obviously, no single collimator is ideal for all scanning applications. The choice of collimator for a given scan will depend upon the sensitivity and resolution requirements, as well as the energy of the radiation.

2. Detector size and thickness

The effects of the diameter of the NaI(Tl) crystal on the sensitivity and resolution of the scanning system have been discussed above. Crystals of 3 inch and 5 inch diameters are the most widely used. However, an 8 inch diameter crystal is available on at least one commercial scanner. The crystal thickness affects the efficiency of the detector. Thicker crystals are more efficient for higher energy gamma rays, up to a point. Most commercial rectilinear scanning systems utilize crystals that are 2 inches thick.

The detector and collimator, along with the photomultiplier tube and preamp, are housed in a single unit, called the probe, which is attached to a motor driven mechanical movement device. This mechanism, along with mechanical stops which define the lateral and longitudinal limits of the scan, causes the probe to traverse the area of interest at a preset speed then move a preset distance perpendicularly and traverse the area in the opposite direction. This process is continued until the area of interest has been covered. Some scanners have mechanical movements which allow scanning in either direction. The gear may be disengaged to allow hand positioning of the probe. The technique of "hand-scanning," as well as that of choosing the proper scan speed and line spacing, is discussed in Chapter XII.

B. Scan Recording Mechanisms

Scan recording mechanisms are of two types--dot recorders and photographic recorders. The dot recorder produces a map of the distribution of activity within the area of interest by recording dots or slitlike marks on paper. The photographic recorder gives the same result on film by photographing the light flashes on the face of a cathode ray tube. This latter method is more versatile because control can be exercised over the intensity, size, and duration of the light flash which exposes the film.

In most commercial scanners, the recording mechanisms are mechanically linked to the scanning head or probe by means of a rigid bar. Consequently, the recorders move simultaneously with and in exact 1-to-1 correspondence to the probe. Some scanners, however, use an X-Y plotter (Chapter VIII) to duplicate the relative position of the probe, i.e., the recorders are attached to the plotting mechanism of the X-Y plotter which moves in direct proportion to the probe.

1. Dot recorders

a. Electronic stylus dot recorder

Figure IX-5 shows a block diagram of a dot recording mechanism which utilizes an electronic stylus to burn a small spot on a sheet of electrical conducting paper each time a pulse passes through the stylus.

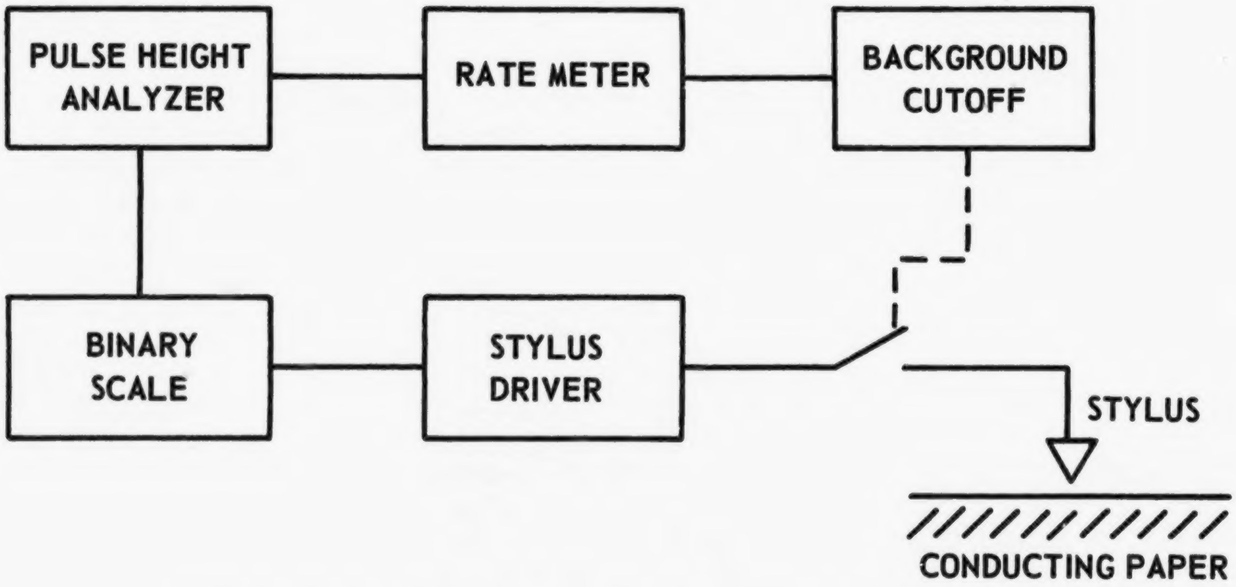

Figure IX-5.--Dot Recording Mechanism Utilizing an Electronic Stylus

Signals from the pulse height analyzer are fed through a binary scaling circuit to a stylus driver which, in turn, sends a signal through the stylus, thus causing a small dot to be burned on the conducting paper. The binary scaling circuit divides the counts from the pulse height analyzer by a factor called the scale factor. The scale factor is adjustable from 1 to 256. A scale factor of eight, for example, means that for every eight counts arriving at the input of the binary scaling circuit from the pulse height analyzer, one is transmitted to the stylus driver, i.e., one dot appears on the paper. This reduction in counting rate is sometimes necessary because extremely high counting rates will paralyze the stylus. Also, the scale factor may be used as a means of emphasizing, on the dot scan, differences between areas of high and low counting rates.

While the signals from the pulse height analyzer are being transmitted digitally to the stylus, they are also being averaged by a count ratemeter. (See Figure IX-5.) The count ratemeter emits an analog voltage signal which is proportional in magnitude to the counting rate. A background cutoff circuit compares this signal with a preset reference voltage signal. Only when the signal from the count ratemeter is greater than the reference voltage is the switch (indicated in Figure IX-5) closed, thereby allowing signals from the stylus driver to be transmitted to the stylus. The magnitude of the reference voltage is determined by adjusting a helipot control on the instrument which is calibrated in per cent of full scale reading. Hence, if the ratemeter range selection switch is set so the full scale meter reading is 3,000 cpm and the background cutoff is set at 10%, then no dots will be recorded on the paper over areas which yield less than 300 cpm. However, as soon as the counting rate goes above 300 cpm then all of the pulses from the stylus driver are recorded in a digital fashion. In other words, the background cutoff does not actually subtract counts, but determines whether all or none of the counts will be recorded.

The ratemeter time constant (see Chapter VIII) does not affect the dot scan except when a background cutoff of greater than zero is used. (When the background cutoff is set at zero, the switch in Figure IX-5 remains closed at all times.) If this is the case, a long time constant will result in a considerable lag time between the detector response and the meter response. The effect of this on the dot scan is discussed in Chapter XII.

b. Dot recorders utilizing mechanical tappers

Some commercial scanners utilize a mechanical rather than an electronic stylus. A mechanical stylus produces an impression in the same manner as a typewriter by striking an inked ribbon against plain white paper. Hence, no special paper is required. The stylus is driven by means of a solenoid which causes it to tap the ribbon very sharply each time a pulse is received from the binary scaling unit. This type of tapper can record up to 7,500 cpm.

Some mechanical tappers are used in conjunction with pressure-sensitive paper to produce a dot scan. Here no ribbon is required since the impact of the tapper striking the paper against a hard surface is sufficient to cause a mark. Special paper is required, however.

c. Color dot recorders

Color dot scans may be obtained from the mechanical tapper recorder by causing the tapper to strike an inked ribbon which moves between the tapper and plain white paper. The ribbon is divided into several bands (usually eight), each of a different color. The analog signal from the ratemeter causes the ribbon to move laterally beneath the tapper as the counting rate changes. The ribbon position is preadjusted before each scan so that the maximum counting rate of interest is represented by a certain color. Thus the counting rate range, from maximum to background, is divided into eight colors.

2. Photographic recorders

The components of a typical photorecording mechanism are shown in Figure IX-6.

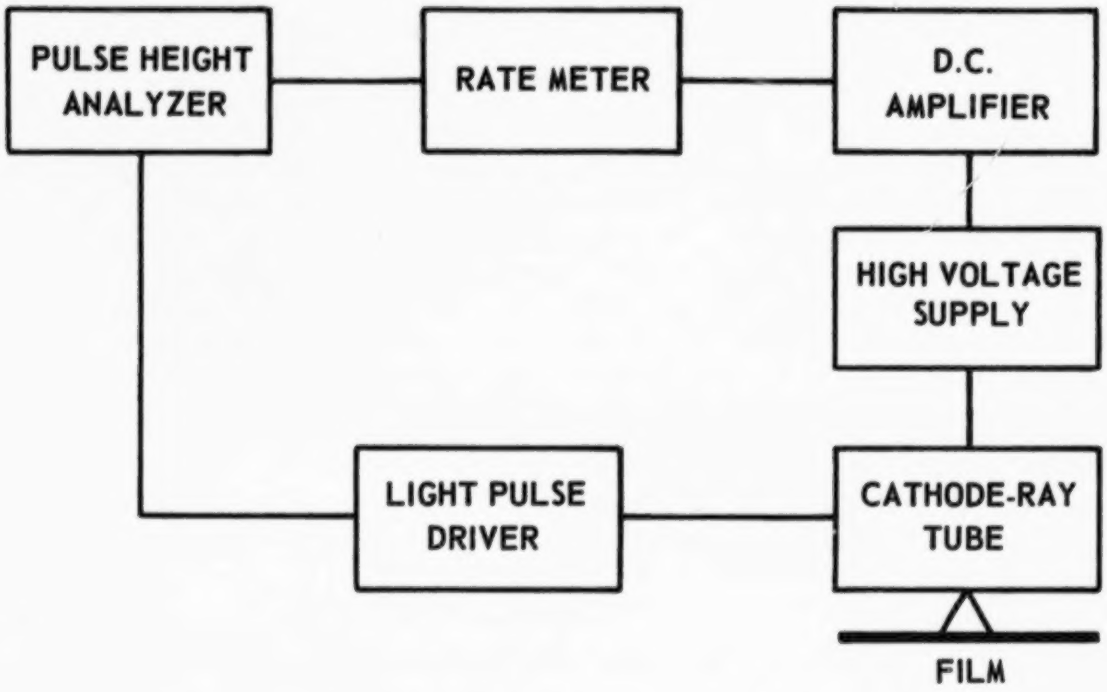

Figure IX-6.--Simplified Diagram of a Scan Photo-Recording Mechanism

Pulses from the pulse height analyzer cause a light source (cathode ray tube [CRT]) to be energized momentarily, thus exposing a small area of photographic film. The effect of the light flash on the film can be controlled in three ways: (1) the size and shape of the area of film exposed for each pulse may be controlled by placing different size and shape apertures between the CRT and the film; (2) the duration of the light flash may be controlled by means of an external setting on the light pulse driver (see Figure IX-6); and (3) the intensity of the light flash may be controlled by modulating the voltage applied to the CRT. The effect of the intensity modulation is called contrast enhancement.

The photographic recorder works as follows: Pulses from the pulse height analyzer are fed simultaneously to the ratemeter and light pulse driver. Each pulse that reaches the light pulse driver causes the CRT to be turned on for a preset period of time determined by an external setting on the light pulse driver. This time is usually between 1 and 150 microseconds, depending on the observed counting rate and scanning speed. Unlike the dot recorder, there is no scaling down of the number of pulses fed to the photorecorder. Thus, there will be superposition of dots on the film. This is desirable on photographic scans because it helps to emphasize differences in isotope concentration within the organs. (The degree of superposition of dots will be greater for areas of high isotope concentration, thus producing a greater overall density on the film.) The light duration must be set so the film density corresponding to the area of maximum counting rate is a reasonable value.

Modulation of the intensity of the light flash with counting rate (contrast enhancement) is accomplished as follows: The ratemeter averages the pulses from the pulse height analyzer over a time period determined by the time constant of the ratemeter (see Chapter VIII). The ratemeter, in turn, produces a dc signal which is proportional in magnitude to the counting rate at any time. This dc signal is then amplified by a factor which is determined by the gain of the dc amplifier in Figure IX-6. On some scanners, this gain setting is externally adjustable, and on others it is preset and remains constant. The signal from the dc amplifier drives the power supply for the CRT. Thus, the voltage applied to the CRT varies in direct proportion to the counting rate. This means that the light flash from the CRT is more intense when the detector is recording over areas of higher isotope concentration.

The gain of the dc amplifier determines the slope of the curve which relates the optical density of the film to counting rate. Optical density (O. D.) = $\log (I_0 \div I)$.

where: I_0 = the intensity of the light incident on the film

I = the intensity of the transmitted light

An O. D. of 2.0 to 2.2 appears totally opaque to the eye, whereas an O. D. of about 0.1 is undistinguisable from the base fog of most films. By adjusting the gain on the dc amplifier, the useful dynamic range of the film (i.e., O. D. = 0.1 to O. D. = 2.2) can be made to extend over any desired counting rate interval. This is accomplished by setting the voltage on the CRT at a value so that the film density corresponding to the maximum counting rate of interest is approximately 2.2. (See Figure IX-7.) Then the dc amplifier gain determines the count rate at which O. D. will be approximately 0.1. In Figure IX-7, the voltage on

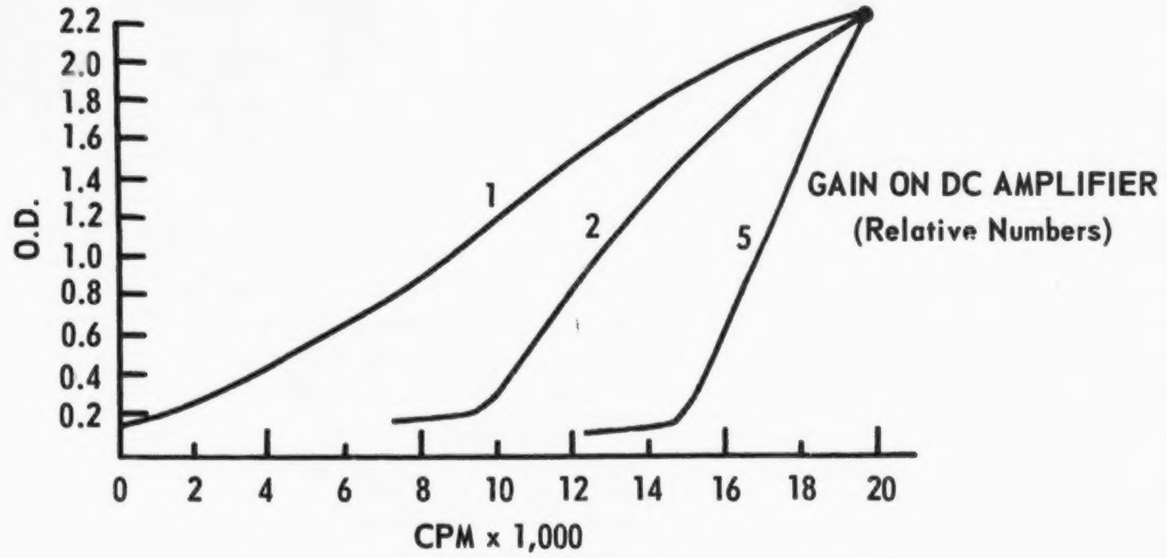

Figure IX-7.--Optical Density vs. Count Rate for Different dc Amplifier Gain Settings

the CRT is set so as to produce an O. D. of 2.2 at 20,000 cpm. With a relative gain setting of 1, the O. D. goes from 2.2 down to 0.1 over the counting rate range of 20,000 cpm to approximately zero cpm. Thus, with this gain setting, even background counts would cause dots of sufficient O. D. so as to be distinguishable from base fog. If the gain is doubled, the useful range of optical densities is limited to the counting rate range of from 10,000 cpm to 20,000 cpm. In this case, no information will be recorded on the film when the detector is over areas which yield less than 10,000 cpm because the light flash will not be of sufficient intensity to produce an optical density distinguishable from base fog. Similarly, as the amplifier gain is increased to 5, the slope of the curve increases, thus further compressing the counting rate range over which information is recorded. This process of increasing the amplifier gain serves to enhance the differences in film density corresponding to differences in isotope concentration--thus the term contrast enhancement. It must be remembered, however, that although the preceding is true, statistical variations in counting rate are also enhanced on the film by the use of very high gain settings. Consequently, the use of contrast enhancement to an excessive degree may cause artificial variations in the optical density of the film.

Scanners with a fixed dc amplifier gain are set so the O. D. reaches 0.1 at zero cpm: i.e., the useful range of the film is spread out over the counting rate range of zero to the maximum counting rate of interest. This way all the pulses from the pulse height analyzer are recorded on film and no information is discarded.

Some scanners have the capability of cutting out the contrast enhancement portion of the photorecorder altogether (i.e., ratemeter and dc amplifier). In this case, the voltage to the CRT remains constant throughout the scan and each mark recorded on the film produces about the same optical density. Film contrast results from differences in the degree of superposition of dots caused by differences in counting rate.

3. Other recording mechanisms

In addition to the routine dot and photoscans, a number of other methods may be used for handling and displaying scan data. One process currently receiving widespread interest is digital recording on magnetic tape. The advantage of this is that the data can be recalled and displayed in a number of ways with varying amounts of background erase and contrast enhancement without destroying the original data. Readout devices available for this include oscilloscopes with a Polaroid camera attachment to integrate the counts and retention oscilloscopes. (Retention or "storage" oscilloscopes have a long decay time phosphor which will hold an image for up to 20 minutes. This allows for visualization of the entire scan on the scope itself.) Data recorded on magnetic tape may be processed by computer to obtain counting rate profiles, etc. Also, closed circuit television may be used to view a photographic scan under different conditions of contrast enhancement by varying the video gain of the system.

III. STATIONARY IMAGING DEVICES AND HIGH-SPEED SCANNERS

During the past few years several attempts have been made to design scanning instruments which have increased sensitivity over the conventional rectilinear scanner yet maintain acceptable resolution. Two types of instruments have emerged--stationary imaging devices which utilize stationary detectors large enough to cover an entire anatomical area of interest, and high-speed multicrystal scanners which are actually rectilinear scanners but are generally regarded as comparable to the stationary imaging devices.

A. Stationary Detector Imaging Devices

Three types of stationary imaging devices are commercially available at present--the scintillation camera, the digital autofluoroscope, and the image converter gamma ray camera.

1. Scintillation camera

a. Detector and positioning electronics

The scintillation camera was developed by H. O. Anger working at the Donner Laboratory, University of California. The commercially available version of the scintillation camera employs an 11½ inch diameter by ½ inch thick NaI(Tl) crystal which is viewed by 19 phototubes in a hexagonal array. Because of the thin crystal, the efficiency for high-energy radiation is low. When a gamma-ray interaction produces light in the crystal, each phototube will respond by producing an electrical signal proportional in magnitude to the intensity of the light incident on its photocathode. Obviously, those phototubes closer to the actual location of the interaction in the crystal will produce a larger signal than those farther away. The result is that each of the 19 phototubes produces a signal which is inversely proportional to the square of its distance from the site of the interaction. Each of these 19 signals is divided into 4 components: X^+, X^-, Y^+, Y^-. These are then added vectorally by means of a capacitor network to form four positioning signals. (See Figure IX-8.) The X^+ and X^- signals are subtracted by means of a difference circuit to yield a resultant X positioning signal. A Y positioning signal is derived in the same manner. These X and Y signals are then applied to the deflection plates of a cathode ray tube in an oscilloscope causing the electron beam to strike the face of the tube in the same relative position as the site of the interaction in the crystal. The four positioning signals are also added to form a Z signal which is analyzed according to height. Consequently, only those pulses that fall within the window of the pulse height analyzer (photopeak pulses) cause light flashes to appear on the face of the cathode ray tube. In more recent models, the difference circuits have been replaced by ratio circuits which divide the resultant X and Y signals by the Z signal. This make the positioning more independent of pulse height and allows the use of wider windows.

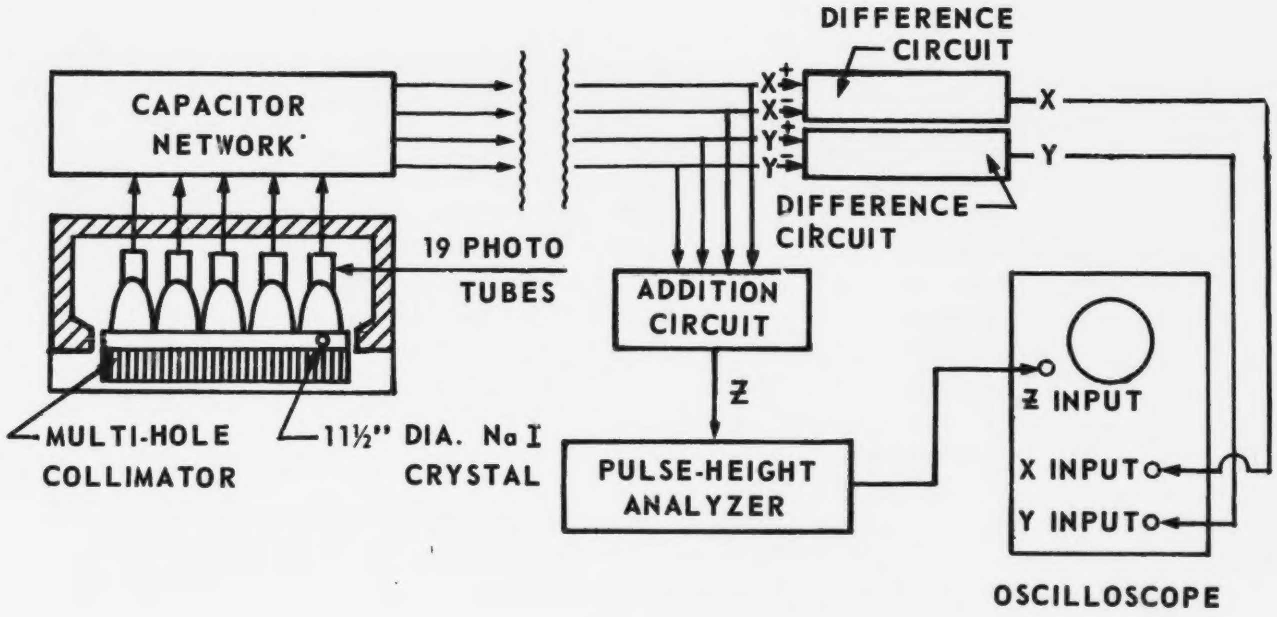
DIFFERENCE CIRCUIT
CAPACITOR NETWORK
X+
X−
Y+
Y−
X
Y
DIFFERENCE CIRCUIT
19 PHOTO TUBES
ADDITION CIRCUIT
Z
Z INPUT
X INPUT
Y INPUT
MULTI-HOLE COLLIMATOR
11½" DIA. NaI CRYSTAL
PULSE-HEIGHT ANALYZER
OSCILLOSCOPE

Figure IX-8.--Simplified Block Diagram Illustrating the Principle of Operation of the Scintillation Camera

A Polaroid camera is mounted onto the oscilloscope and the film integrates the dots as they appear on the face of the cathode ray tube. The intensity of each dot is adjusted by an external control on the oscilloscope. Anywhere from 10,000 to several hundred thousand dots can be recorded per picture, depending upon the type of study performed.

b. Collimators

Two types of collimators are used with the scintillation camera--a multiple hole, straight-bore collimator, and a pinhole collimator. The straight-bore collimator is used to visualize larger organs, such as the liver, brain, etc.; the pinhole collimator is used for small areas, such as the thyroid gland.

Commercially available straight-bore collimators are of two types: the 1,000 hole collimator, with relatively thick lead septa, is used with high-energy gamma emitters, and a 4,000 hole collimator is available for use with low-energy gamma emitters. Unlike the focusing collimator used with rectilinear scanners, the point of best resolution of a straight-bore collimator is at its surface.

The pinhole collimator, designed specifically for thyroid work, works on the same principle as a pinhole camera (see Figure IX-9.) Instead of light rays passing through a pinhole in an opaque box and producing a latent image on photographic film, gamma rays from a radioactive source concentrated in the thyroid gland pass through a pinhole in a lead collimator and interact in the NaI crystal. The collimation is not as perfect for gamma rays as it is for light and some radiation will penetrate the collimator. The pinhole collimator is available with three pinholes arranged to produce two oblique views of the thyroid, as well as a straight anterior view.

2. Digital autofluoroscope

The digital autofluoroscope, developed in 1962, is a stationary imaging device designed to be more efficient for high-energy photons while maintaining the high sensitivity of the scintillation camera.

a. Detector-collimator

The detector consists of 294 sodium iodide crystals, each $\frac{3}{8}$ inches in diameter and 2 inches thick. These are hexagonally placed in a 6 X 9 inch array, with 1 cm center-to-center spacing. The 2 inch thick crystals provide a two-fold increase in efficiency over a $\frac{1}{2}$ inch thick crystal for 365 keV photons of ^{131}I. This factor is not so important for lower-energy gamma rays.

The collimator is a 3 inch thick lead block pierced by 294 conical apertures--one for each crystal. The apertures are tapered from $\frac{1}{4}$ inch on the crystal side to $\frac{1}{8}$ inch on the patient side.

The resolution of the system is equal to the resolution of the crystal array. Point sources, placed in adjacent collimator apertures, are resolved as two distinct areas of activity on the display oscilloscope.

b. Data transfer and presentation

In the early model of the autofluoroscope, electronic positioning and pulse height analysis were accomplished in the same manner as with the

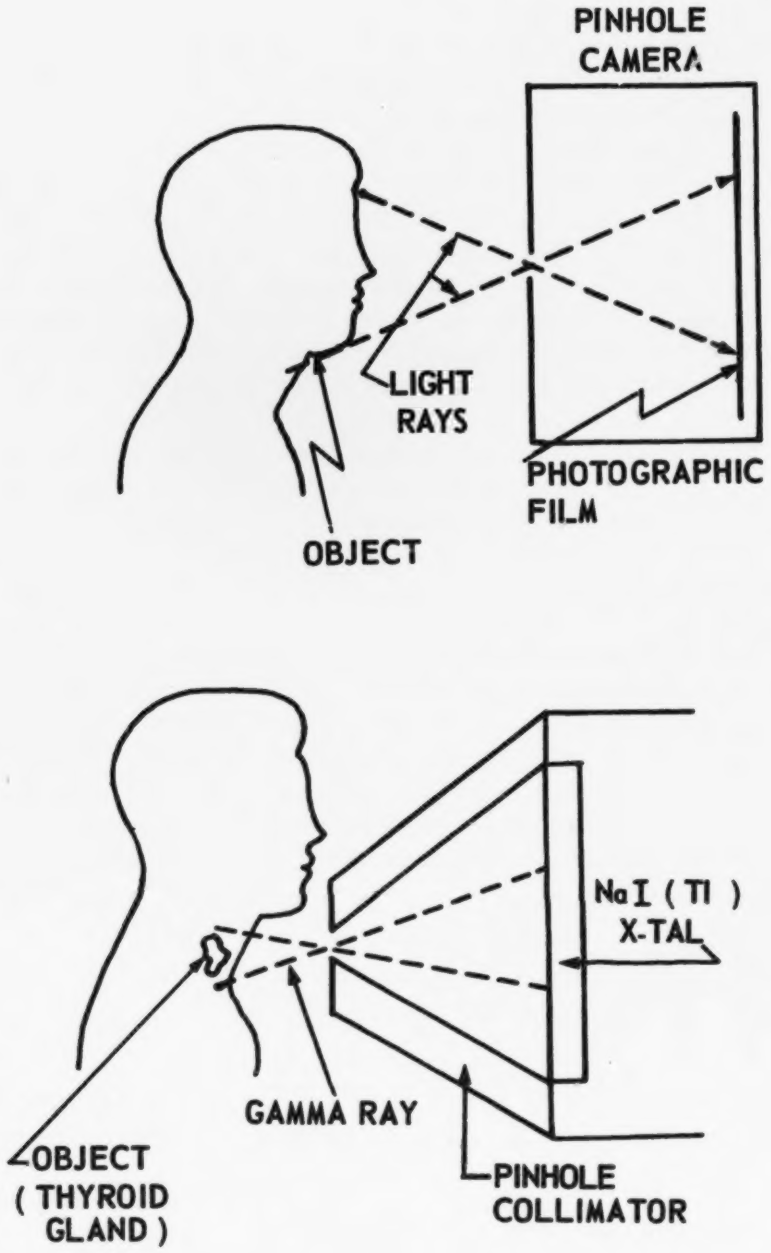
PINHOLE CAMERA
LIGHT RAYS
PHOTOGRAPHIC FILM
OBJECT
NaI (Tl) X-TAL
GAMMA RAY
OBJECT (THYROID GLAND)
PINHOLE COLLIMATOR

Figure IX-9.--Pinhole Collimator

scintillation camera. A more recent version uses a rank and file coincidence method to determine in which of the 294 crystals a particular gamma ray is detected. Then the counts from each crystal are recorded, in digital form, in a magnetic core memory system. The data can then be read out nondestructively on a retention oscilloscope with any desired amount of background erase. The system allows for integration of counts over selected areas of the scan, and for recording the counting rates from these areas as a function of time.

3. Image-converter gamma-ray camera

In 1963, a camera was developed to record the image (of low-energy gamma emitters) shown on an 8 inch image-amplifier tube. This tube has a thin phosphor inside a glass envelope which is sensitive to x rays and low-energy gamma rays. A multihole straight-bore collimator is used to project an image of the subject on the phosphor. When a photon interacts within the phosphor, light is emitted which causes electrons to be ejected from the photosensitive surface of the phosphor. These electrons are accelerated and focused onto a smaller phosphor-coated screen resulting in more intense light flashes. The intensified flashes may be integrated on Polaroid film or the image may be viewed instantaneously on a monitor by means of an Orthicon system.

This instrument is for use only with low-energy photons, such as the 27 keV x rays from ^{125}I. The detection efficiency of the phosphor is very low for medium- and high-energy gamma rays.

B. High-Speed Rectilinear Scanner

Another approach to increasing the sensitivity of a scanning system, without sacrificing resolution, is to use a multicrystal detector with a focusing collimator for each detector. Such a scanner is available commercially. Ten NaI crystals are arranged side-by-side with a distance of 1 inch between centers. Each crystal has its own focusing collimator and phototube, as shown in Figure IX-10. The entire detector assembly moves across the patient, scanning 10 lines at once, 1 inch apart.

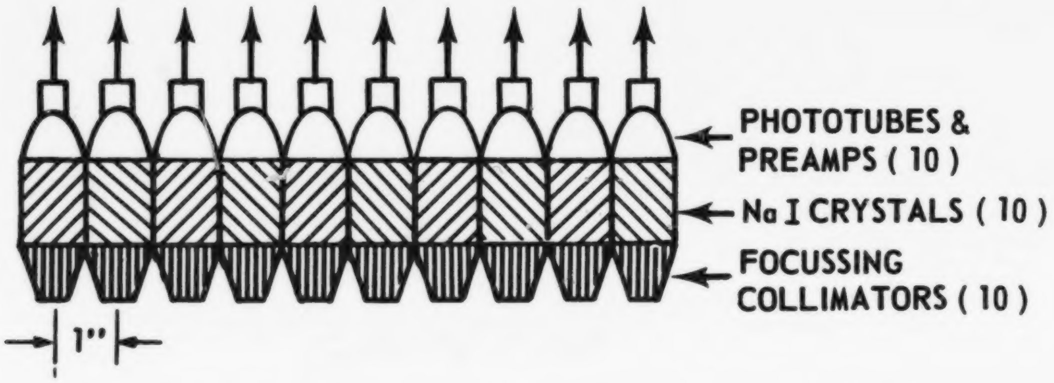

Figure IX-10.--Ten Crystal High-Speed Rectilinear Scanner Detector Assembly

The detector assembly then moves a preset longitudinal distance and traverses in the opposite direction, etc., until the spaces between the original 10 scan lines have been filled in. In this manner, large organs can be scanned in a fraction of the time required with a conventional rectilinear scanner. The time savings for scanning small organs and glands is not as great.

Obviously, to obtain a life-size photographic scan directly would necessitate having 10 photoscanners traversing the film simultaneously. Instead, the output from each phototube is analyzed separately and the counts are stored on magnetic tape. Then, the data can be recalled nondestructively in any one of a number of ways previously discussed, viz., oscilloscope with Polaroid camera attachment, retention oscilloscope, or closed circuit television.

IV. POSITRON SCANNING

The annihilation photons from positron absorption (Chapter V) may be utilized to pinpoint the location of the absorption event in tissue. Advantage is taken of the fact that the annihilation photons are emitted back-to-back and simultaneously. Thus, two detectors stationed at 180° relative to each other may be used, in conjunction with a coincidence circuit (see Chapter VIII) to detect annihilation events. Figure IX-11 illustrates the general arrangement of such a system. Of the three annihilation events pictured as occurring in the source, only "B" will result in an output pulse from the discriminator, since it is the only one which results in a 0.51 MeV photon being absorbed in each crystal. Consequently, the two pulses arrive at the inputs of the coincident circuit simultaneously and an output pulse results.

Any rectilinear scanner or imagine device which allows for detectors mounted on opposite sides of the patient may, with the appropriate electronic modifications, be used for positron scanning. No collimation is necessary. The resolution is determined by the size of the crystals.

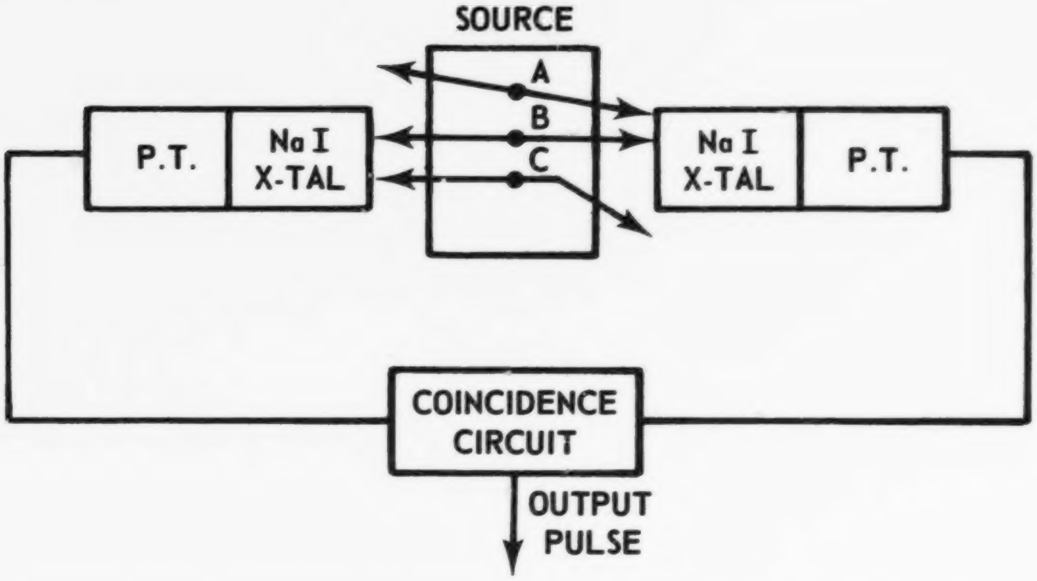

Figure IX-11.--Block Diagram of a Positron Scanning System

The sensitivity of this system is more nearly uniform throughout the region between the two crystals than is the case with the single-detector, focusing-collimator arrangement. In the case of the scintillation camera with a commercially available positron attachment, it is possible to obtain a tomographic effect, i.e., one plane is in sharp focus while the other planes are superimposed but blurred. The plane of best focus can be set to any desired level by adjusting an attenuator in the electronic circuits.

Positron scanning has received its greatest use in brain studies. Isotopes that have been used for this purpose are: ^{74}As, ^{64}Cu, ^{68}Ga, and ^{18}F, among others. One disadvantage to these materials, compared to ^{99m}Tc and other "pure" gamma emitters, is the increased patient dose from the absorption of the particulate radiation. Positron scanning is not a frequently used technique at this time.

SUGGESTIONS FOR FURTHER READING

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2. Blahd, W. H., Nuclear Medicine, McGraw-Hill Bock Co. (1965), pp. 43-69.

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CHAPTER X

NUCLEAR COUNTING STATISTICS

I. INTRODUCTION

The statistical nature of radioactive decay was recognized soon after the discovery of radioactivity. In fact, the law of radioactive decay (Chapter III) can be deduced strictly from statistical considerations, proving it a statistical relationship subject to the laws of chance. Hence, in any sample containing a large number of radioactive atoms, some average number will disintegrate per unit time. But the exact number which disintegrate in any given unit of time fluctuates around the average value. In counting applications, it is important to estimate this fluctuation because it indicates the repeatability of results of a measurement.

II. FREQUENCY DISTRIBUTIONS

If one plots the frequency of occurrence of values against the values themselves for a series of identical measurements of a statistical process, a curve will result--the frequency distribution curve. Many statistical phenomena conform to certain standard frequency distributions. If this distribution is known, certain inferences about a population may be made by observing a small sample of the population. In nuclear counting statistics, frequency distributions of interest are the normal, the Poisson (pronounced PWAH-SOHN'), and the chi-square distributions.

A. Normal Distribution

The normal distribution describes most statistical processes having a continuously varying magnitude. If one plots the frequency distribution curve for a large number of measurements on a quantity which conforms to the normal distribution, a familiar bell-shaped curve (similar to the one shown in Figure X-1) will result. This is the normal distribution curve. It is characterized by two independent parameters: the mean (m) and the standard deviation (σ).

1. Mean

The mean is the average value of the quantity under observation. For the standard normal distribution (i.e., symmetrical about the mean), the mean value is the one that occurs with the highest frequency. Since in reality we observe only a portion of the population, we estimate the mean by a numerical average ($\bar{x}$).

$$\bar{x} = \frac{\sum x_i}{n} \qquad (1)$$

where x_i is the value of the i^{th} measurement, n is the total number of observations.

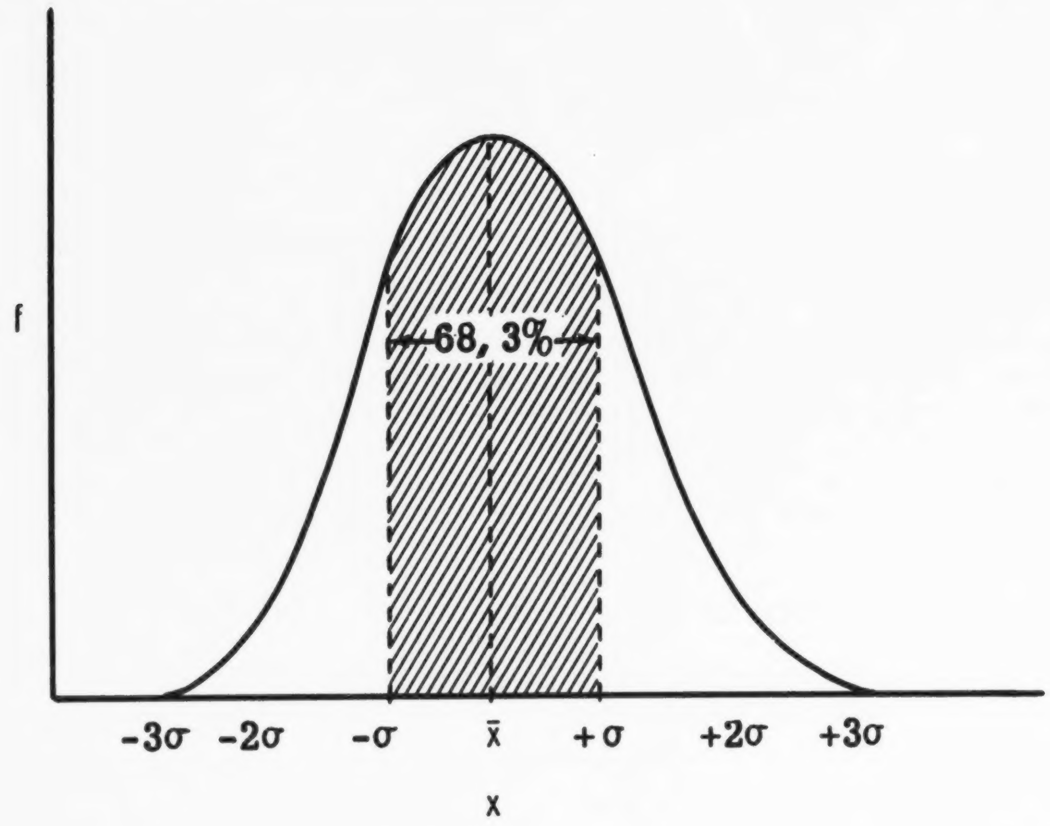

Figure X-1.--Normal Distribution Curve

2. Standard deviation

The standard deviation is defined as the square root of the average of the squares of the individual deviations from the mean. Expressed mathematically, this is

$$\sigma = \sqrt{\frac{\sum (x_i - m)^2}{n}} \qquad (2)$$

where m is the mean value, x_i is the value of the i^{th} measurement, and n is the total number of observations. As with the mean, we must estimate σ from a finite number of observations. The best estimate of σ is called s_x which is given by

$$s_x = \sqrt{\frac{\sum (x_i - \bar{x})^2}{n - 1}} \qquad (3)$$

The use of n - 1 in the denominator results from the use of ($\bar{x}$) instead of m in the numerator. In other words, we lose one degree of freedom by estimating m with $\bar{x}$. Since m and σ are independent parameters which characterize the normal distribution, it is possible to have an infinite number of values of σ for a given mean. However, the smaller the standard deviation, the greater the reproducibility of the measurements. If one covers one standard deviation on each side of the mean of a standard normal distribution curve, approximately 68% of the total area under the curve will be included. (See Figure X-1.) Two standard deviations on each side of the mean include approximately 95% of the total area, three standard deviations--99.7%, etc. The practical significance of this is: If one estimates the mean of a series of normally distributed measurements by $\bar{x}$, and estimates the standard deviation by s_x, it can be said with 68% confidence that the true mean value of the quantity lies between $\bar{x} \pm s_x$. Likewise, it can be said with 95% confidence that the true mean is somewhere between $\bar{x} \pm 2s_x$, etc.

B. Poisson Distribution

The Poisson distribution equation is:

$$P(x) = \frac{e^{-m} m^x}{x!} \qquad (4)$$

where P(x) is the probability that a given value in a series of observations will occur x times. The Poisson distribution adequately predicts the frequency distribution resulting from the observation of a large number of events which, taken singly, have a small but constant likelihood of occurrence. The Poisson distribution is characterized by only one parameter--the mean. If the definition of standard deviation (II.A.2) is applied to the Poisson distribution equation, the following expression results:

$$\sigma = \sqrt{m} \qquad (5)$$

Thus, the standard deviation for the Poisson distribution depends on the mean. It can have only one value for a given mean value. Another difference between the normal and Poisson distributions is that m and x must be integers in the Poisson distribution, while the normal distribution is a continuous one.

It can be shown that radioactive decay obeys the Poisson distribution law. If one observes a sample containing a large number of radioactive atoms for a period of time which is short compared to the half-life, then the probability that a single atom will decay during the observation time is small but constant for equal time intervals. Also, only integer numbers of atoms decay in any time period. Hence, nuclear disintegrations obey Poisson statistics. If, however, the mean number of observed events is moderately large, say 100 or more, the Poisson distribution is adequately approximated by a special normal distribution for which $\sigma = \sqrt{m}$, or in terms of our estimates of these parameters,

$$s_x = \sqrt{\bar{x}} \qquad (6)$$

The approximation is usually considered acceptable if the mean value is 20 or greater. This is the preferred method for handling nuclear counting data, since it is less complex than working with the Poisson distribution directly.

III. APPLICATION TO NUCLEAR COUNTING DATA

The following symbols will be used throughout the remainder of this chapter:

N = total counts

t = counting period

$n = \frac{N}{t}$ = count rate

The subscript, g, refers to the sample plus background count (gross count), b refers to the background count alone, and s refers to the net sample count. Naturally, s must be obtained by subtraction, since it is impossible to observe directly the sample activity apart from the ever-present background.

A. Standard Deviation in Total Count (N)

From Equation (6) the standard deviation in the total sample plus background count, s_{N_g}, is given by

$$s_{N_g} = \sqrt{N_g} \tag{7}$$

and the standard deviation in the total background count, s_{N_b}, is calculated from

$$s_{N_b} = \sqrt{N_b} \tag{8}$$

B. Standard Deviation in Count Rate (n)

To obtain the standard deviation in the gross count rate, divide both sides of Equation (7) by the counting period. Then,

$$s_{n_g} = \frac{s_{N_g}}{t_g} = \sqrt{\frac{N_g}{t_g^2}} = \sqrt{\frac{N_g}{t_g} \times \frac{1}{t_g}} \tag{9}$$

But, $\frac{N_g}{t_g} = n_g$

Therefore, the standard deviation in the gross count rate, s_{n_g}, is calculated as follows:

$$s_{n_g} = \sqrt{\frac{n_g}{t_g}} \tag{10}$$

Similarly, the standard deviation in the background count rate, s_{n_b}, is given by

$$s_{n_b} = \sqrt{\frac{n_b}{t_b}} \tag{11}$$

C. Standard Deviation in Net Count Rate (n_s)

The net count rate, n_s, is given by

$$n_s = n_g - n_b$$

Notice the count rates are used, because total counts cannot be subtracted unless the counting period is the same for sample and background. This is rarely the case. The problem here is one of combining the standard deviations in the gross count rate and the background count rate. The method of combining standard deviations $s_{x_1} + s_{x_2}$ to obtain the standard deviation in the sum or difference of two measurements $x_1 \pm x_2$ is:

$$s_{x_1 \pm x_2} = \sqrt{s_{x_1}^2 + s_{x_2}^2} \qquad (13)$$

Thus, by combining Equations (10) and (11), one obtains the following expression for s_{n_s}, the standard deviation in the net count rate:

$$s_{n_s} = \sqrt{\left(\sqrt{\frac{n_g}{t_g}}\right)^2 + \left(\sqrt{\frac{n_b}{t_b}}\right)^2} = \sqrt{\frac{n_g}{t_g} + \frac{n_b}{t_b}} \qquad (14)$$

Example:

Given the following data, find the standard deviations in (a) the total gross and background counts, (b) the gross and background count rates, and (c) the net count rate. Report (c) at the 95% confidence level.

N_g = 40,000 counts, t_g = 10 min.

N_b = 3,600 counts, t_b = 20 min.

(a) $s_{N_g} = \sqrt{40{,}000} = 200$ counts

$s_{N_b} = \sqrt{3{,}600} = 60$ counts

(b) $n_g = \frac{40{,}000}{10} = 4{,}000$ cpm

$n_b = \frac{3{,}600}{20} = 180$ cpm

$s_{n_g} = \sqrt{\frac{4{,}000}{10}} = 20$ cpm

$s_{n_b} = \sqrt{\frac{180}{20}} = 3$ cpm

(c) $s_{n_s} = \sqrt{(20)^2 + (3)^2} = \sqrt{409} = 20.3$ cpm

Therefore, $n_s = 3{,}820 \pm 40.6$ cpm at the 95% confidence level.

D. Fractional Standard Deviation and Per Cent Uncertainty

It is sometimes convenient to express the uncertainty in a measurement as a fraction of the quantity itself. This is called the fractional standard deviation (FSD) and is determined as follows for the net count rate:

$$(\text{FSD})_{n_s} = \frac{ks_{n_s}}{n_s} = \frac{k}{n_s}\sqrt{\frac{n_s}{t_s} + \frac{n_b}{t_b}}$$

where k is the number of standard deviations required to give the desired confidence level. The uncertainty expressed as a percentage of the total is obtained by multiplying the FSD by 100. In the previous example,

$$(\text{FSD})_{N_s} = 40.6 \div 3{,}820 = 0.0106$$

The uncertainty in the determination is 1.06% of the net count rate at the 95% confidence level.

E. Other Useful Parameters

1. Most probable error

The quantity commonly referred to as the most probable error is the deviation which corresponds to that value which will probably be exceeded on repeat measurements. In other words, it corresponds to the value which, if taken on each side of the mean, will include 50% of the area under the normal distribution curve. Expressed in terms of the standard deviation, the most probable error is equal to $0.6754\ \sigma$.

2. Nine-tenths error

The nine-tenths error is the uncertainty which is expected to be exceeded 10% of the time on repeat measurements; it is $1.64\ \sigma$.

F. The Chi-Square Test of Goodness of Fit

One of the most important applications of statistics to measurements is the investigation of whether or not a particular set of measurements fit an assumed distribution. The test most often used for this purpose on nuclear counting data is Pearson's chi-square test.

The quantity χ^2 is defined as follows:

$$\chi^2 = \sum \frac{[(\text{observed value})_i - (\text{expected value})_i]^2}{(\text{expected value})_i}$$

where the summation is over the total number of independent observations. The expected values are computed from any assumed frequency distribution. For nuclear counting data the assumed distribution is the Poisson, hence the expected value is equal to $\bar{x}$, the average number of counts recorded per interval. Thus

$$\chi^2 = \sum_{i=1}^{n} \frac{(x_i - \bar{x})^2}{\bar{x}} \qquad (15)$$

where n values of x are observed.

The data should be subdivided into at least five classifications, each containing at least five counts.

The steps in applying Pearson's chi-square test to counting data are as follows:

1. Compute $\bar{x} = \frac{\Sigma x_i}{n}$.

2. Compute χ^2 from Equation (15).

3. Determine the degrees of freedom (F).

   F is the number of ways the observed distribution may differ from the assumed. In our application, F = n - 1.

4. From Table X-1, with the values of χ^2 and F, determine P.

   P is the probability that larger deviations than those observed would be expected due solely to chance if the observed distribution is actually identical to the assumed distribution. From this definition, it is obvious that too little deviation is possible as well as too much. The closer P is to 0.5, the better the observed distribution fits the assumed, for larger deviations than those observed are just as likely as not. The interpretation of P is for $0.1 \le P \le 0.9$, the observed and assumed distributions are very likely the same. If $P < 0.02$ or if $P > 0.98$ the equality of the distributions is very unlikely. Any other value of P would call for additional data to better define the observed distribution.

An example of the use of Pearson's test is as follows: The data in the following table are from a series of ten 2 minute counts of a standard source made with a G-M laboratory counter. We wish to determine whether these data reflect proper instrument operation. The chi-square test is applied as shown on page 113.

TABLE X-1.--Table of Chi-Square Values*

Number of Determinations	Probability						
	0.99	0.95	0.90	0.50	0.10	0.05	0.01
3	0.020	0.103	0.211	1.386	4.605	5.991	9.210
4	0.115	0.352	0.584	2.366	6.251	7.815	11.345
5	0.297	0.711	1.064	3.357	7.779	9.488	13.277
6	0.554	1.145	1.610	4.351	9.236	11.070	15.086
7	0.872	1.635	2.204	5.348	10.645	12.592	16.812
8	1.239	2.167	2.833	6.346	12.017	14.067	18.475
9	1.646	2.733	3.490	7.344	13.362	15.507	20.090
10	2.088	3.325	4.168	8.343	14.684	16.919	21.666
11	2.558	3.940	4.865	9.342	15.987	18.307	23.209
12	3.053	4.575	5.578	10.341	17.275	19.675	24.725
13	3.571	5.226	6.304	11.340	18.549	21.026	26.217
14	4.107	5.892	7.042	12.340	19.812	22.362	27.688
15	4.660	6.571	7.790	13.339	21.064	23.685	29.141
16	5.229	7.261	8.547	14.339	22.307	24.996	30.578
17	5.812	7.962	9.312	15.338	23.542	26.296	32.000
18	6.408	8.672	10.085	16.338	24.769	27.587	33.409
19	7.015	9.390	10.865	17.338	25.989	28.869	34.805
20	7.633	10.117	11.651	18.338	27.204	30.144	36.191
21	8.260	10.851	12.443	19.337	28.412	31.410	37.566
22	8.897	11.591	13.240	20.337	29.615	32.671	38.932
23	9.542	12.338	14.041	21.337	30.813	33.924	40.289
24	10.196	13.091	14.848	22.337	32.007	35.172	41.638
25	10.856	13.848	15.659	23.337	33.196	36.415	42.980
26	11.524	14.611	16.473	24.337	34.382	37.382	44.314
27	12.198	15.379	17.292	25.336	35.563	38.885	45.642
28	12.879	16.151	18.114	26.336	36.741	40.113	46.963
29	13.565	16.928	18.939	27.336	37.916	41.337	48.278
30	14.256	17.708	19.768	28.336	39.087	42.557	49.588

*Usually tables in statistical texts give the probability of obtaining a value of χ^2 as a function of df, the number of degrees of freedom, rather than of n, the number of replicate determinations. In using such texts, the value of df should be taken as n-1.

x_i	$(x_i - \bar{x})^2$
264	144
267	225
242	100
261	81
233	361
247	25
237	225
263	121
243	81
263	121
2,520	1,484

$$\bar{x} = \frac{2,520}{10} = 252$$

$$\chi^2 = \frac{1,484}{252} = 5.9$$

$$F = 10 - 1 = 9$$

From Table X-1, $P \approx 0.72$. Thus, we conclude that the data reflect proper instrument operation.

G. Minimum Detectable Activity

Minimum detectable activity (MDA) is defined as the activity (usually in microcuries) which will result in a count rate significantly different from background for a given counting time. If the sample counting time is to equal the background counting time, $\text{MDA} = (k \div f)\sqrt{N_b \div t_b}$, where k is the number of standard deviations corresponding to the chosen confidence level, and f is the calibration factor for the instrument (f has units of cpm/μCi).

H. Application of Statistics to Ratemeter Readings

In a manner completely analogous to the derivation of the standard deviation in the count rate from an integral counter, the following expression may be derived for an instantaneous ratemeter reading:

$$s_r = \sqrt{\frac{r}{2\ RC}}$$

where r is the ratemeter reading in counts per minute or counts per second, and RC is the time constant of the ratemeter in appropriate time units.

IV. STATISTICAL CONTROL CHARTS

One way to continually check the accuracy and precision of a nuclear counting instrument is with statistical control charts. A statistical control chart permits a periodic check to see if the observed fluctuation in the counting rate from a constant source of radioactivity is consistent with that predicted from statistical considerations. To construct such a chart, it is necessary first to make 20 or 30 independent measurements of the same source, keeping the counting time constant. Then a chi-square test must be performed on this data to insure proper instrument operation at the outset. Once proper operation is established, the mean counting rate and the standard deviation are calculated from the data. Next, a graph is constructed as shown in Figure X-2, and daily counting rates are plotted.

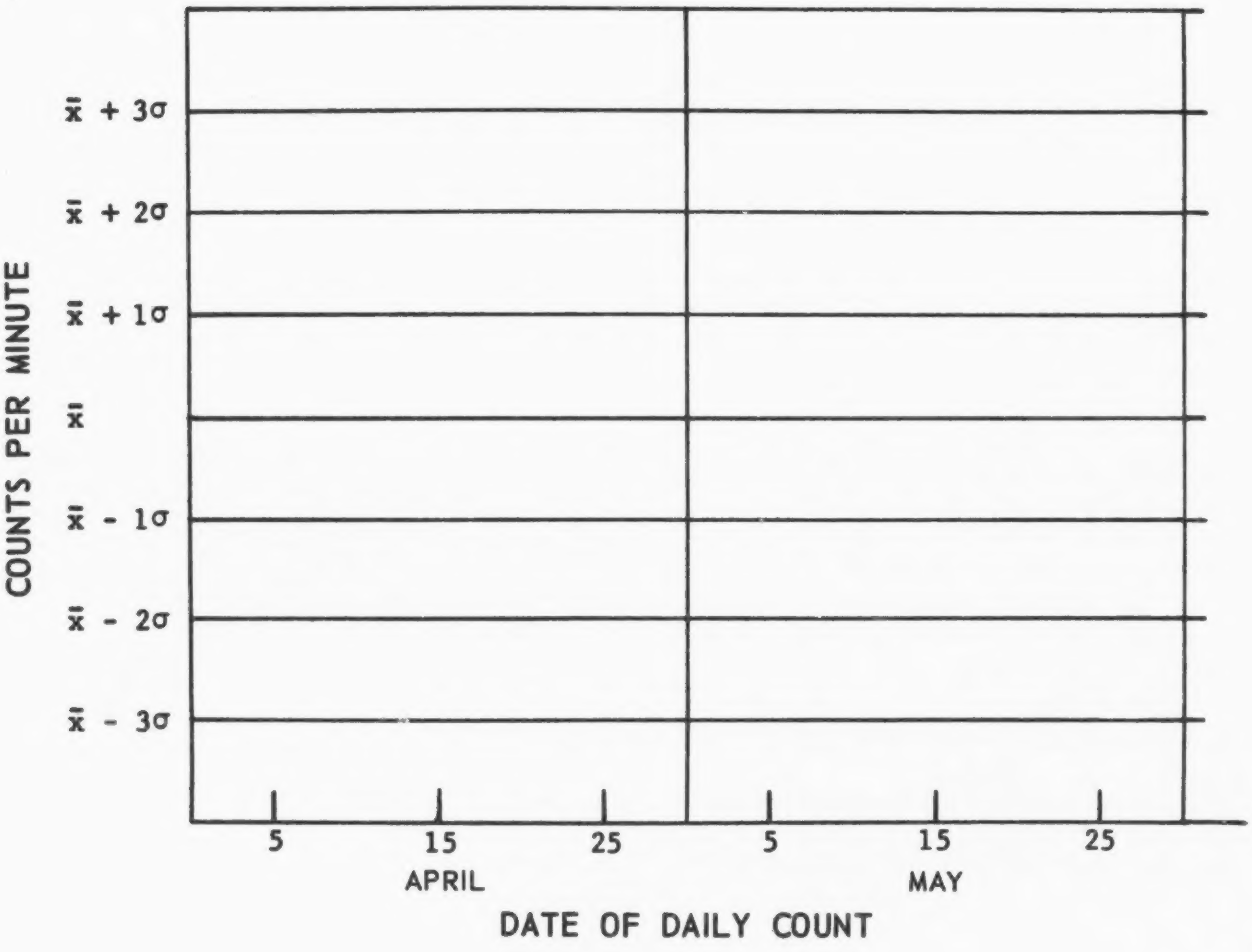

Figure X-2.--Control Chart

It is wise to label the abscissa in calendar units to facilitate retrospective analyses. Individual deviations from the mean should not exceed one standard deviation more than 33% of the time, two standard deviations more than 5% of the time, etc. If a measurement falls outside the 95% (2σ) line it should be repeated. Since there is one chance in 20 that a single value will fall outside these limits by chance alone, the chances are one in 400 that such will be the case on two successive observations. Hence two successive measurements outside the 95% control limit is sufficient cause to suspect anomalous data. One should also watch for trends in the data, i.e., gradual but consistent changes in either direction.

One readily available source for constructing statistical control charts is the ever-present background radiation. It is important to measure background at least daily on a routinely used instrument, since certain causes of erroneous data (e.g., contamination and external sources in the area) are reflected in changing background count rates.

V. SUMMARY

The application of statistics to nuclear counting data is mandatory to the precision with which measurements are made. It should be emphasized that only the uncertainty due to the random nature of the decay process is considered in this chapter. If other significant sources of uncertainty are present, such as timing, they must be dealt with separately and included in the overall estimate of the accuracy.

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CHAPTER XI

PRINCIPLES OF IN VITRO COUNTING

I. INTRODUCTION

Counting applications may be divided into two categories: in vitro and in vivo. In vitro counting refers to samples of materials that are counted outside the living organism, e.g., blood, urine, feces, etc. Such samples are usually prepared in a test tube, planchet, or other convenient counting vial (vitro means glass) and counted in some type of laboratory counting system. In vivo counting here refers to the assessment of radioactivity in all or some selected part of the living organism. In vivo counting will be discussed in Chapter XII.

II. ABSOLUTE COUNTING

This term means the absolute disintegration rate of a sample will be determined rather than simply the relative counting rate. It permits a quantitative assessment of the sample's radioactivity.

A. Overall Efficiency

In order to do absolute counting, the overall efficiency of the counting system must be known. Overall efficiency (E) is defined as follows:

$$E = \frac{\text{cpm}}{\text{dpm}}$$

Hence, the sample disintegration rate is obtained by dividing the relative count rate by the efficiency factor. Several factors affect the overall efficiency of a counting system.

1. Geometry

The prime factor affecting the efficiency of any counting system is the position, size, and shape of the sample relative to the sensitive volume of the detector. This relationship determines the geometry of the counting arrangement. (Geometry is defined as the fraction of the solid angle about a source which is subtended by the sensitive volume of the detector. Hence, geometry is dependent on the size and shape of both the source and the detector.)

a. End-window detectors

In the simple case of an end-window detector with radius r used to count a point source (see Figure XI-1), the geometry factor (G) is easily determined from the above definition:

$$G = \tfrac{1}{2}\,(1 - \cos\alpha)\text{, or}$$

$$G = \tfrac{1}{2}\left(1 - \frac{h}{\sqrt{h^2 + r^2}}\right)$$

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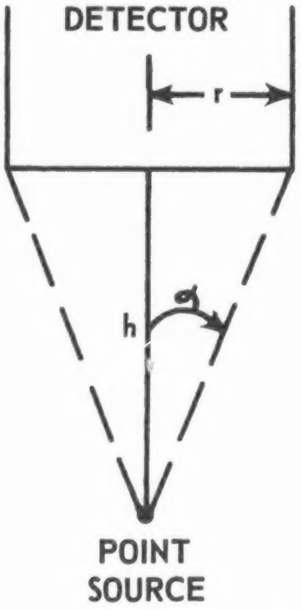

Figure XI-1.--Detector Geometry

where h is the perpendicular distance from the source to the detector. The geometry factor changes rapidly with the distance h for small values of h. At large distances ($h \gg r$), the geometry factor varies as the inverse square of the distance.

b. Internal detectors

In certain gas-ionization detectors, the sample is placed inside the sensitive volume (Chapter VII). These are either "2π" or "4π" counters; i.e., the detection chamber is either hemispherical or spherical; hence either one-half or all the solid angle about the source is subtended by the detector. Thus, from the definition of geometry, the geometry factors for 2π and 4π counters are 0.5 and 1.0, respectively.

c. Well counters

Scintillation crystals may be constructed with a "well" in the center of the crystal as shown in Figure XI-2. This type of detector allows the counting of samples in test tubes or similar counting vials. Figure XI-2 shows that the geometry factor for a point source in a well counter is given by:

$$G = \tfrac{1}{2}\,(1 + \cos\alpha), \text{ or}$$

$$G = \tfrac{1}{2}\left(1 + \frac{h}{\sqrt{h^2 + r^2}}\right)$$

where: h = distance from the source to the top of the crystal

r = radius of the well as measured from the centerline to the edge of the crystal.

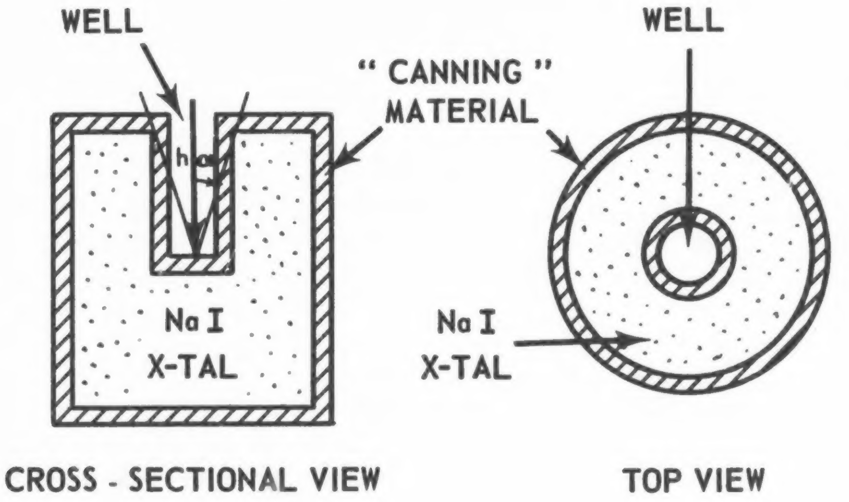
WELL
" CANNING "
MATERIAL
h
α
Na I
X-TAL
WELL
Na I
X-TAL
CROSS - SECTIONAL VIEW
TOP VIEW

Figure XI-2.--Well Type NaI Detector

d. Other counting geometries

Other counting arrangements are often used for in vitro counting, such as the Marinelli beaker in which a liquid sample partially surrounds the detector. The calculation of geometry factors for this and other extended source arrangements is complex, and will not be presented here.

2. Absorption

Another factor that affects overall efficiency is radiation absorption by the window or wall materials of the detector and by the sample itself. Self-absorption in the sample is especially important for alpha and beta counting and for very low-energy gamma rays. Window or wall absorption is most important for particulate radiation, but may also be significant for low- and medium-energy gamma rays, depending on the thickness and composition of the material. When alpha particles are counted with an end-window counter, even the air between the sample and detector window will cause significant absorption and must be kept to a minimum.

Self-absorption (absorption by the sample) of particulate radiation may be determined experimentally by counting several samples of equal activity but different density-thicknesses (expressed in mg/cm^2). (See Chapter V.) If this is done for different isotopes--each having a different maximum beta energy--a family of curves is obtained, as shown in Figure XI-3. For each energy there is a point beyond which additional sample thickness does not affect the counting rate. This thickness is called the saturation thickness and is equal to the density-thickness in mg/cm^2 which corresponds to the maximum range of the beta particles. Window absorption effects may be determined by placing absorbers of different thicknesses between the sample and detector and plotting a curve for each beta energy. The curves can be extrapolated to zero thickness and the ratio of observed counting rate to the counting rate without absorption can be determined.

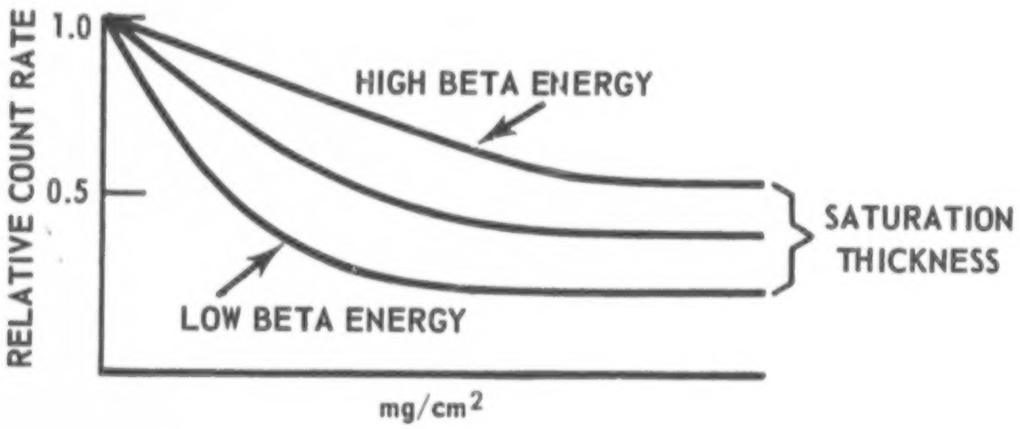

Figure XI-3.--Relative Count Rate vs. Sample Density-Thickness for Different Maximum Beta Energies

3. Scatter

Scattering from sample mounts and shielding may significantly increase a counting rate above what it would be if it were somehow suspended in air with no scattering material present. This contribution is nil for alpha particles--and also for gamma rays if only photopeak pulses are counted. It may be significant in integral gamma counting, but the contribution due to scatter is most important for high-energy beta particles where the counting rate may be increased by as much as 60 to 70% due to scatter from the sample mount. The scatter contribution may be determined experimentally by making a plot of counting rate vs. density-thickness of the sample mount. This yields a curve of the type shown in Figure XI-4. The counting rate increases with increasing mg/cm^2 up to the point at which the density-thickness of the sample mount is equal to one-half the maximum range of the beta particle. This is called the saturation thickness of the sample mount. The scatter contribution is a function of the atomic number of the sample mount as well as its density thickness and the beta energy.

4. Intrinsic efficiency

Geometry, absorption, and scatter determine the fraction of the photons or particles emitted by the sample that will enter the sensitive volume of the detector. The term intrinsic efficiency is defined as the ratio of the number of photons or particles that interact in the detector to the number that enter the sensitive volume. For most detectors, the intrinsic efficiency is 100% for alpha and beta particles, i.e., the detecting medium is of sufficient volume and sufficient density so that all charged particles that enter the medium interact and cause ionization. The intrinsic efficiency for gamma rays, however, is dependent on photon energy as well as on the size and shape of the detector, the detecting medium, and the distance from the source to the detector. With gamma

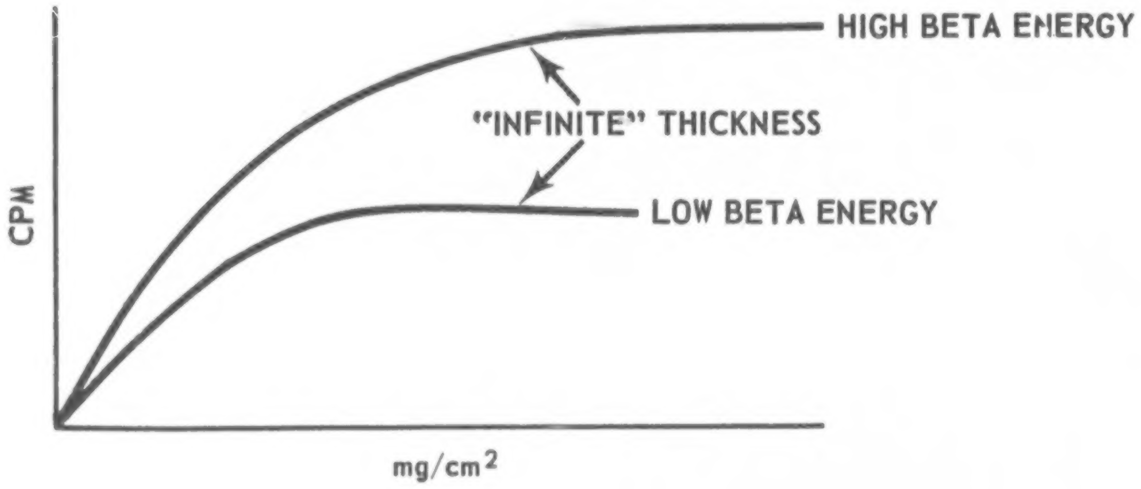

Figure XI-4.--Relative Count Rate vs. mg/cm^2 of Sample Mount for Different Beta Energies

radiation, a given value for intrinsic efficiency must be specified for the entire pulse height spectrum, or for photopeak counts only. The latter representation is called intrinsic peak efficiency. The intrinsic peak efficiency vs. photon energy for a NaI(Tl) crystal 1½ inches in diameter by 1-inch thick with a point source at 7 cm from the detector is given in Figure XI-5. Over a limited energy range, the intrinsic peak efficiency is proportional to the photon energy raised to a constant negative power.

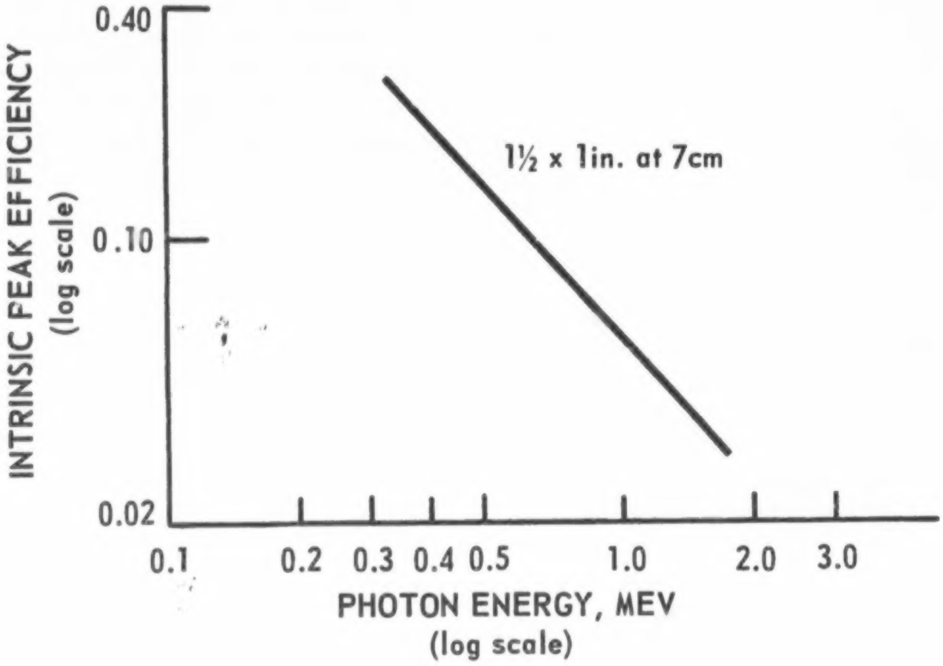

Figure XI-5.--Intrinsic Peak Efficiency vs. Photon Energy for a 1½ X 1-inch NaI (Tl) Crystal

Hence, for constant geometry and detector dimensions, the intrinsic peak efficiency decreases very rapidly with increasing photon energy.

The intrinsic peak efficiency for gamma photons is also proportional to the volume of the detector and the atomic number of the detecting medium; the value for NaI is approximately 100 times greater than that for G-M counting gas.

Overall efficiency is the product of the four factors discussed above: geometry, absorption, scatter, and intrinsic efficiency. For relatively simple counting arrangements, these individual factors may be calculated or determined experimentally as shown. But for most counting applications involving volume sources, these factors are difficult to determine accurately. So the preferred method for determining overall efficiency is usually by means of a standard source, whose absolute disintegration rate is known to a high degree of accuracy. Efficiency E is then calculated according to the expression, E = cpm/dpm. This may be expressed as a calibration factor f, with units of cpm per microcurie as follows:

$$f\left(\frac{\text{cpm}}{\mu\text{Ci}}\right) = 2.22 \times 10^6\ E$$

where E is the overall efficiency as previously defined.

If possible, the standard should be the same isotope as is in the sample being assayed. Also, the geometry, absorption, and scatter factors should be the same for the standard as for the unknown samples, e.g., identical sample mounts, equal volumes, etc.

With short-lived isotopes, an accurately calibrated standard source cannot be maintained. A long-lived isotope with similar properties, with regard to the types and energies of the emissions, must be substituted. Examples include the use of ^{57}Co as a substitute for ^{99m}Tc, and a combination of ^{137}Cs and ^{133}Ba to simulate ^{131}I.

When a different isotope is used as a standard for counting gamma emissions, the per cent abundance of the gamma ray of interest must be determined for both isotopes, and the activity of the standard corrected to compensate for any difference in per cent abundance. For example, every 100 disintegrations of ^{99m}Tc results in 99 photons of 140 keV energy. However, the yield for the 123 keV photon from ^{57}Co is only 93 per 100 disintegrations. Thus, it takes 99 ÷ 93 millicuries of ^{57}Co to yield the same number of photons as 1 millicurie of ^{99m}Tc. If ^{57}Co is to be used as a standard for ^{99m}Tc, the ^{57}Co activity must be expressed in terms of equivalent technetium activity.

B. Instrument dead time

Instrument dead time is defined as the time following the occurrence of a pulse during which the instrument is insensitive to incoming radiation. This may be thought of as the time required for the instrument to "recover" from one event to the point that another pulse may be processed.

1. Correction

To estimate the true counting rate for a given time interval, the observed counting rate must be corrected for dead time losses. The following symbols are used

τ = dead time (microseconds)

n_o = observed counting rate

n_t = true counting rate

then,

$n_t - n_o$ = number of counts lost per unit of time due to dead time. (1)

Also,

$n_0 \tau$ = the fraction of the counting interval during which the instrument is not recording.

Then,

$n_t \times n_0 \tau$ = the number of counts lost per unit time due to dead time. (2)

Hence, equating (1) and (2),

$$n_t - n_0 = n_t \times n_0 \tau$$

Solving this equation for n_t yields,

$$n_t = \frac{n_0}{1 - n_0 \tau} \qquad (3)$$

This equation may be used to calculate the true counting rate if the dead time is known.

Example:

Typical dead time for a G-M instrument is 100-200 microseconds. Calculate the true counting rate if the observed rate is 50 counts/sec., and the dead time is 200 microseconds. Repeat the calculation for an observed counting rate of 200 counts per sec.

Solution:

$$\text{From (3)} \quad n_t = \frac{n_0}{1 - n_0 \tau} = \frac{50}{1 - (50)\ (200 \times 10^{-6})}$$

$$n_t = 50.5 \text{ counts/sec.}$$

Note that the uncorrected counting rate is in error by only 1%. Hence, dead time losses are relatively unimportant in this example. Solving the same equation for a count rate of 200 counts per second yields

$$n_t = \frac{200}{1 - (200)\ (200 \times 10^{-6})}$$

$$n_t = 555 \text{ counts/sec.}$$

In this example, the uncorrected counting rate is in error by 11%.

These examples show that correcting for dead time losses becomes more important with increasing counting rates. Also, it should be noted that dead time is a statistical phenomenon subject to the same laws of chance as is radioactive decay.

2. Experimental determination of dead time

The following is known as the split-source method of determining dead time. Only two sources that can be counted both separately and simultaneously under constant conditions of geometry, scatter, etc., are needed.

Let

n_1 = observed gross counting rate from source 1

n_2 = observed gross counting rate from source 2

n_{12} = observed gross counting rate from 1 and 2 counted simultaneously

n_b = background counting rate

Then, the true counting rate from source 1 is equal to:

$$\frac{n_1}{1 - n_1\tau}$$

and similarly for the others. The following equality may be written:

$$\frac{n_{12}}{1 - n_{12}\tau} + \frac{n_b}{1 - n_b\tau} = \frac{n_1}{1 - n_1\tau} + \frac{n_2}{1 - n_2\tau} \qquad (4)$$

The background term on the left side is necessary because two backgrounds are included in n_1 and n_2 counted separately. Equation (4) is difficult to solve exactly for τ, but may be adequately approximated as follows:

$$\tau \approx \frac{n_1 + n_2 - n_{12} - n_b}{n_{12}^2 - n_1^2 - n_2^2}$$

Typical dead times for various detectors are:

G-M tube	100 to 200 microseconds
proportional counter	0.2 to 0.5 microseconds
scintillation detector	0.001 to 0.01 microseconds.

These values are associated with the detector itself. In the case of scintillation detectors, the dead time for the instrument is determined by the speed with which the associated electronics can process the pulses, since the recovery time of the scintillation phosphor is much faster than the electronics. In G-M instruments and most proportional counters, the detector itself is the limiting factor. Dead time corrections are necessary only when doing quantitative measurements using calculated efficiency values, or when comparing relative counting rates which differ widely from one another.

C. Double Isotope Quantitative Determinations

Independent quantitative measurements of two or more isotopes in a single sample may be made using gamma ray pulse height analysis if the energies of the gamma rays are sufficiently different from each other. Let E_1 represent the gamma ray energy of isotope #1, and E_2 the energy of isotope #2. Assume each isotope emits only one gamma energy. Also let ΔE_1 represent the window (energy interval) used to count isotope #1 alone, and ΔE_2 the window for isotope #2 counted alone. As seen from Figure XI-6, the photopeak at E_1 will contain counts arising from the scatter of the E_2 gamma, and ΔE_2 may contain counts from the E_1 gamma.

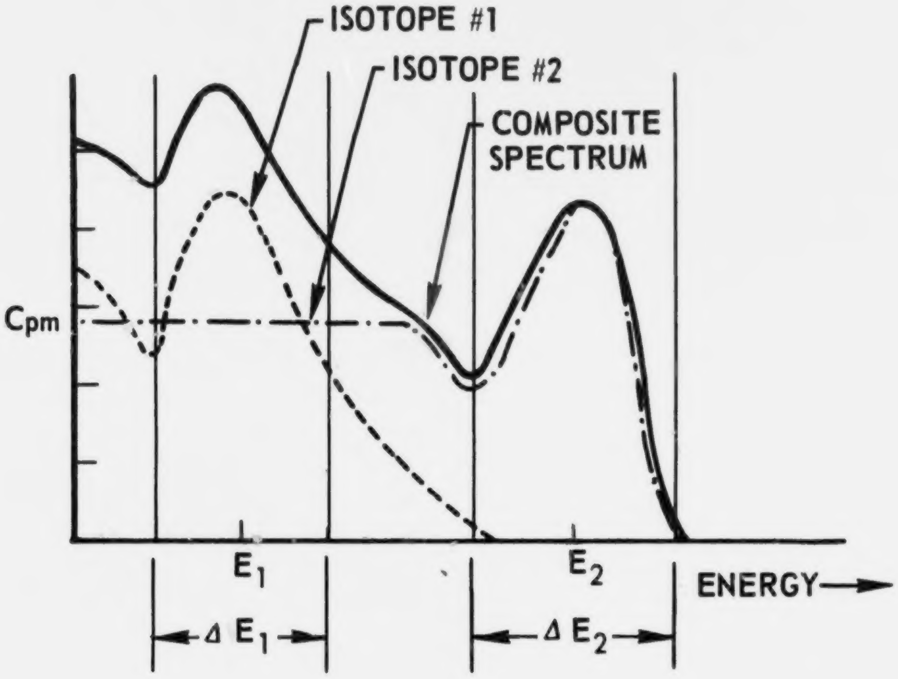

Figure XI-6.--Individual and Composite Sprectra for Two Single-Energy Gamma-Emitting Isotopes in a Single Sample

Symbols used are here defined:

C_1 = calibration factor (cpm/μCi) for isotope #1 in ΔE_1

C_2 = calibration factor for isotope #2 in ΔE_2

f_1 = calibration factor for isotope #2 in ΔE_1

f_2 = calibration factor for isotope #2 in ΔE_2

n_1 = counting rate in ΔE_1

n_2 = counting rate in ΔE_2

A_c = activity (microcuries) of isotope #1

A_f = activity (microcuries) of isotope #2.

From the definition of the calibration factor,

$$n_1 = A_c C_1 + A_f f_1$$

Similarly,

$$n_2 = A_c C_2 + A_f f_2$$

Solving these two equations simultaneously for A_c and A_f yields,

$$A_c = \frac{n_1 f_2 - n_2 f_1}{C_1 f_2 - C_2 f_1}$$

and

$$A_f = -\frac{n_1 C_2 - n_2 C_1}{C_1 f_2 - C_2 f_1}$$

The calibration factors must be determined experimentally using standard sources counted under identical conditions of geometry, scatter, etc. as the unknown sample. For this method to be valid, the two gamma energies must be far enough apart so windows wide enough to give statistically valid counting rates may be used without appreciable overlap.

III. RELATIVE COUNTING

Many applications in nuclear medicine require only relative comparisons of, say, several counts done on the same sample at different times, or the counting rates of many different samples. In this case, no overall efficiency determination is necessary. It is important, however, that all individual factors that determine overall efficiency (geometry, transmission, and absorption) be kept constant for all samples to be intercompared. Since the dead time correction is dependent on counting rate, it is necessary to make this correction, even in relative counting applications, when the counting rates to be compared differ widely.

IV. SUMMARY

In vitro counting applications may require knowledge of either the absolute disintegration rate of a sample or merely the relative counting rates of several samples. For absolute determinations, the overall efficiency of the counting system must be ascertained by comparison with a standard source, or, if feasible, calculation of the individual factors that determine overall efficiency. Dead time corrections, where significant, should be applied to all counting data.

SUGGESTIONS FOR FURTHER READING

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CHAPTER XII

PRINCIPLES OF IN VIVO COUNTING

I. INTRODUCTION

In vivo counting applications involve direct measurement of the radioactivity within a living organism--in clinical nuclear medicine, a human being. Such studies may be divided into two broad categories: distributive counting, detection of radioactivity in a particular organ; and whole-body counting, measurement of the total amount of radioactivity in the body. Apart from superficial beta activity, only gamma rays and bremsstrahlung radiation are detectable outside the body. The remarks in this chapter apply mainly to gamma-emitting radionuclides (positron emitters included because of the annihilation photons from positron absorption).

II. DISTRIBUTIVE COUNTING

Studies requiring measurement of radioactivity in a selected organ may be divided into three categories, based on the type of information sought. These are quantitative determinations, scanning, and kinetic studies.

A. Quantitative Measurements

Quantitative assessment of the radioactivity in a human organ is basically no different from quantitative assessment of in vitro samples. The same factors determine the overall efficiency--geometry, absorption, scatter, and the intrinsic efficiency of the detector. But these factors are--with the exception of intrinsic efficiency--much more difficult to control in in vivo counting. Also, since it is almost impossible to accurately calculate from first principles the overall efficiency of an in vivo counting arrangement, mock-up studies with phantoms containing a known amount of radioactivity must be made. Accurate reproduction of the efficiency factors--geometry, absorption, and scatter, in the phantom mock-up is the major problem in in vivo quantitative measurements. In addition, a phantom-standard source arrangement which accurately simulates one person's gamma-ray spectrum may not be accurate for another with different physical characteristics. It is difficult to obtain calibration factors applicable to large numbers of individuals. Some sources of variability in the efficiency factors are:

1. Geometry

The geometry of in vivo counting arrangements is determined by the size of the organ, the area of the detector, the distance from the source to the detector, and the length and diameter of the collimator. As discussed in Chapter XI, when the detector is very close to the source, the response of the detector is strongly dependent on the distance between the two. At greater distances this dependence is not as pronounced. Hence, the effect on geometry of small variations in the depth of an organ within the body becomes less with increasing distance from the detector. For this reason, it is sometimes necessary to sacrifice sensitivity by moving the detector away from the source to minimize error due to small changes in geometry. A case in point is the thyroid uptake study.

Detector size and collimation for in vivo counting should allow the entire volume of interest to be included in the detector's field of view while excluding as much surrounding tissue as possible. This insures that the number of photons recorded from the volume of interest relative to the total number recorded will be maximal. In some instances (e.g., thyroid uptake) it may be necessary to measure separately the contribution from the surrounding tissue and subtract this from the total count. Two methods commonly used for this purpose are:
(a) Counting with a lead shield covering the area of interest; then the difference between this and the total count is taken as the true organ count. (b) Counting over a similar anatomical area (e.g., the thigh to simulate the athyroidal neck). Both methods leave much to be desired as far as accuracy is concerned. But considering the magnitude of other measurement errors, these are generally tolerated.

2. Absorption and scatter

Radiation absorption and scatter by both the volume of interest and surrounding tissue depend on the size and shape of the volume, depth of the volume within the body, molecular composition of the tissue within the volume of interest as well as that of the surrounding tissue, and the energy of the radiation. Since the intrinsic efficiency of gamma-ray detectors is strongly dependent on photon energy, a phantom with a standard source that simulates the shape of the entire pulse height spectrum obtained from the patient is important. This is particularly important if integral counting is done. If only photopeak counts are recorded, a less accurate phantom mock-up is tolerable. Common materials used to simulate the gamma ray attenuation properties of soft tissue include water, presswood, masonite, lucite, and various other types of plastics.

B. Scanning

Radioisotope scanning graphically shows the distribution of radioactive material within an organ, gland, or other space in the body. Scanning instrumentation is discussed in Chapter IX. Presented here is a discussion of the way technical factors associated with scanning affect the final result.

1. Information density of scan

A prime consideration in obtaining a good scan is the amount of information required to show statistically significant differences in isotope concentration. Consider the count rates from two equal volumes of tissue, A and B, in which a radioisotope is uniformly distributed. Since the scan is a two-dimensional representation of radioactivity distribution, the two volumes can be compared by the number of counts recorded per unit area (information density) traversed by the scanner, assuming scanning speed remains constant. Under these conditions, one can say (with 95% assurance) that the isotope concentration in B is significantly different from that of A if $|n_A - n_B| \geq 2\sqrt{n_A}$ where n_A and n_B are the counts recorded over unit areas in volumes A and B, respectively. This may be expressed as a fraction of the counts per unit area in A and plotted against the same value. (See Figure XII-1.) This figure, multiplied by 100, is the percentage difference that must exist between the counts per square cm recorded over the two volumes in order to call the difference "significant," according to the chosen criterion.

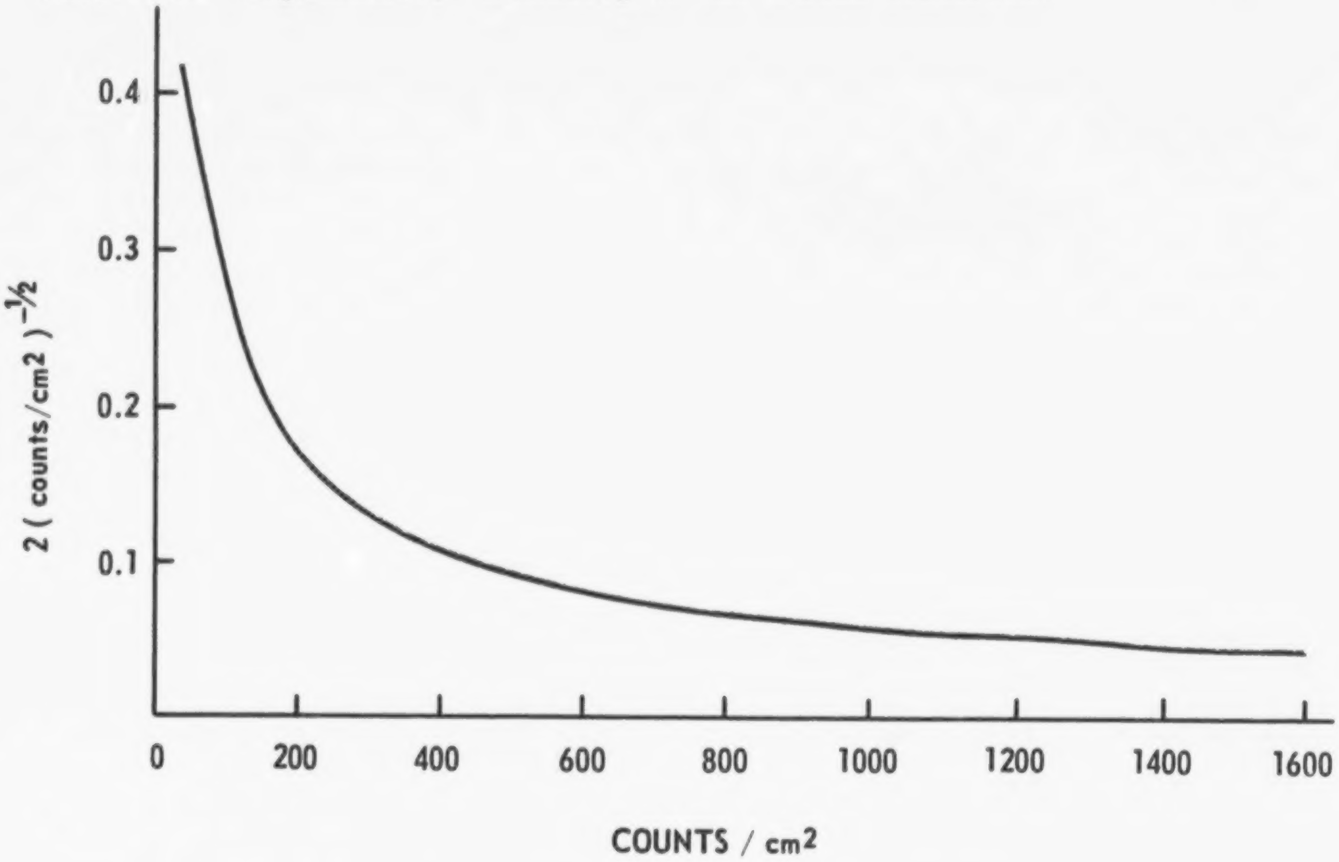

Figure XII-1.--Significant Difference Graph

The graph shows that, in order for an area to be significantly different from one which yields 100 counts/cm^2, the difference between the two must be 20%. A 10% difference will be significant if 400 counts/cm^2 are recorded, 7% for 800 counts/cm^2, etc. The increase in statistical accuracy is less marked as one goes above 800 counts/cm^2. For this reason, some feel that 800 counts/cm^2 recorded over the area of maximum isotope concentration is optimal. Others consider it worthwhile to record up to 1,800 counts/cm^2, particularly when doing "cold-spot" scanning, as with liver, kidney, and thyroid. In practice, a compromise is necessary between information density and time requirements. The high photon flux from short-lived pure gamma emitters such as ^{99m}Tc has resulted in a tremendous increase in the information density of scans without increased scanning time.

It must be emphasized that the foregoing discussion refers only to the rates at which counts are recorded. Other factors, such as contrast enhancement, affect the appearance of the scan image. Unless a statistically significant difference exists in the amount of information recorded between two volumes of different isotope concentration, no valid difference can be shown on the scan.

The information density (counts/cm^2) of a rectilinear scan is determined by the counting rate, scanning speed, and line spacing. The relationship is:

$$\text{information density} = \frac{\text{counts per minute}}{\text{speed (cm/min)} \times \text{line spacing (cm)}} \qquad (1)$$

For a stationary imaging device, the average information density may be obtained by dividing the total number of counts collected by the area scanned. In imaging devices that provide for the integration of counts over selected areas of the field of view, the information density may be determined for any desired area. Conversely, the number of counts to be collected may be calculated from the desired information density.

2. Scanning speed

The scanning speed (cm/min) for rectilinear scanners may be calculated from Equation (1). That is,

$$\text{scanning speed} = \frac{\text{counts per minute}}{\text{information density} \times \text{line spacing}} \qquad (2)$$

Example:

A liver scan is to be performed using ^{99m}TcS as a colloid. The maximum counting rate observed by "hand-scanning" the liver (moving the probe by hand to locate the area of highest counting rate) is 12,000 cpm. The desired information density over the area of highest counting rate is 800 counts/cm^2. Calculate the scanning speed if the line spacing is 0.30 cm. From Equation (2),

$$\text{scanning speed} = \frac{12{,}000 \text{ cpm}}{800 \text{ counts/cm}^2 \times 0.30 \text{ cm}}$$

$$\text{scanning speed} = 50 \text{ cm/min.}$$

3. Line spacing

Line spacing, like scanning speed, applies only to rectilinear scanning. It is normally set equal to the longitudinal dimension of the light spot.

4. Choice of collimator

Collimator properties are discussed in Chapter IX. An infinite number of combinations of sensitivity and resolution are possible in collimator design. In practice, however, the choice is simplified. Of the collimators available with a given commercial rectilinear scanner, usually four or five provide enough versatility for clinical work. These usually include a "coarse," "medium," and "fine" focus for medium and high energy radiation (>200 keV); and a "medium" and "fine" focus for low energy (<200 keV). In terms of numbers of holes for,--say--a 3 inch diameter crystal, standard figures are 19 holes for the coarse focus medium and high energy collimator, either 31 or 37 holes for the medium focus, and 61 holes for the fine focus. Low-energy collimators for a 3 inch crystal typically contain 73 holes. Some specially constructed low-energy collimators have as many as 1,000 holes. The increased number of holes in low energy collimators is possible because thinner septa are permissible than is the case for higher energy photons.

From the choices available, one must also consider the inverse relation between sensitivity and resolution. For routine studies, this usually boils down to: with scans of relatively small, thin structures such as the thyroid gland, the collimator with the smallest resolution distance is generally used commensurate with the energy of the gamma ray. Resolution distance is defined as the width of the 50% isoresponse line measured at the focal plane. For scans of larger, thicker organs such as the liver and brain, one usually chooses a collimator that allows for greater sensitivity and additional depth response. Much work has been done in recent years to arrive at objective criteria for determining the best combination of detector size and collimator for a given scan. Some have proposed a figure-of-merit which is proportional to the likelihood of observing a lesion of a certain size in a given time with a given isotope concentration in the lesion relative to its surroundings. The results of such work indicate that the optimum collimator is one with a resolution distance approximately equal to the diameter of the lesion of interest.

5. Contrast enhancement

It is often difficult to tell, solely on the basis of the counting rates, whether a given area on a photoscan reflects a significantly different isotope concentration from its surroundings. In such cases, it is possible to modulate the intensity of the light spot (as discussed in Chapter IX) to emphasize real differences in counting rates. There must be sufficient information on the scan so the use of contrast enhancement does indeed emphasize existing differences in counting rates and does not create artificial ones. A high degree of contrast enhancement on a low information density scan may emphasize statistical variation to the point of making a homogeneous source of radioactivity look very heterogeneous.

Count-rate modulation of the light source intensity is not generally done on stationary imaging devices as it is on rectilinear scanners. But a similar effect can be achieved by photographing the cathode-ray tube through multiple lenses, each with a different aperture opening.

6. Time constant

The ratemeter time constant affects both the rectilinear dot recording and the photoscan when background cutoff and contrast enhancement are used. Too long a time constant causes the scan lines to be offset from one another at the edges of the scan. This is called "scalloping." Also, small areas of increased or decreased isotope concentration may be obscured by using a too-long time constant. With the dot scan, the time-constant dependence stems from the fact that the recorder records information only when the counting rate exceeds the background cutoff level. (See Chapter IX.) Thus, if the counting rate suddenly exceeds this level, and a long time constant relative to the scanning speed is used, the probe may be well into the area of interest before the ratemeter has responded enough to energize the recorder.

A similar effect is obtained on the photographic scan when contrast enhancement is used. Here scalloping is the result of modulation of the light source, whose intensity lags behind the actual changes in counting rate when too long a time-constant is used.

On the other hand, an excessively short time constant will yield poor statistical accuracy for the average value of the dc signal which controls the light intensity. This results in a "salt and pepper" effect on the photographic scan. This is caused by excessive fluctuation of the ratemeter reading. There is merit in using as long a time constant as possible, commensurate with the required scanning speed.

The proper value for the time constant depends on the scanning speed and the diameter of the area to be delineated. Specifically, the time constant must be small compared with the time required for the detector to traverse this area. This time is given by d/s where d is the diameter of interest in cm and s is the scanning speed in cm/min. A rule of thumb is that the ratemeter be allowed to go through ten time constants during the time d/s; or RC = 0.1 d/s.

Example:

A thyroid scan is to be performed at a speed of 15 cm/min. The limit of the resolution for a cold nodule is approximately 0.5 cm. What time constant should be used?

The time required for the detector to transverse 0.5 cm is:

$$\frac{0.5\text{ cm}}{15\text{ cm/min}} = 0.033\text{ min} = 1.98\text{ sec.}$$

Using the rule of thumb,

$$RC = \frac{1.98\text{ sec}}{10} \approx 0.2\text{ sec.}$$

In practice, one is limited to a few choices of time-constant settings. Hence, a single setting is usually applicable for all scans of a given type unless unusual circumstances arise.

C. Kinetic Studies

The advent of radiopharmaceuticals has greatly facilitated in vivo observation of dynamic physiologic processes. Such studies require accurate recording of the rate at which the tagged material enters and leaves one or more compartments in the body. The time scales of interest range from seconds (in certain blood flow studies) to weeks, months, or even years in some long-term retention studies. In the latter, the change in the distribution of the radionuclide is negligible during the period of a single observation. Also, studies of this type are often carried out in a whole-body counter, discussed in the next section. Instrumentation factors important in observing a process which is changing rapidly during the time of observation are discussed here. Examples include renal, hepatic, and cerebral blood flow studies, and cardiac output studies, among others.

1. Geometry

Since many kinetic studies do not require quantitative measurements, precise reproduction of the geometry from one patient to another is not vital. Hence, to improve sensitivity, the face of a straight bore collimator is generally placed in contact with the skin directly over the volume of interest. It is important, however, to also maximize the ratio of the number of photons detected from the volume of interest to the number detected from other tissues and background. This involves finding the optimum collimator length to crystal-diameter ratio for the volume of interest.

2. Data recording

After processing by a pulse height analyzer, the pulses are averaged over a finite time interval, and the information is recorded. The manner in which this is done is crucial to the proper representation of the true kinetic phenomenon by the recorded data.

a. Analog ratemeter with strip-chart recorder

Traditionally, the most widely used instrument for recording data from kinetic studies has been the analog ratemeter strip-chart recorder combination. (See Chapter VII.) Selection of the proper ratemeter time constant is extremely important. In Chapter VII a discussion was given of the exponential nature of the response of an analog ratemeter. It is worthwhile here to discuss the case where the counting rate itself is changing exponentially. Here, the ratemeter cannot fully respond to one change in counting rate before another change occurs. The fact that the counting rate is continually changing means that the ratemeter response is never going to fully catch up to the true counting rate. Also, the time lag between the actual change in counting rate and the ratemeter response is dependent on the frequency of the change. It has been demonstrated that a time constant equal to $1/5\lambda$, where λ is the rate constant for the true change in counting rate, will adequately reproduce the shape of the true curve if only relative information is desired. For studies requiring integration under the counting rate curve (e.g., cardiac output), even this short time constant ($1/5\lambda$) may cause a significant error in the quantitative determination.

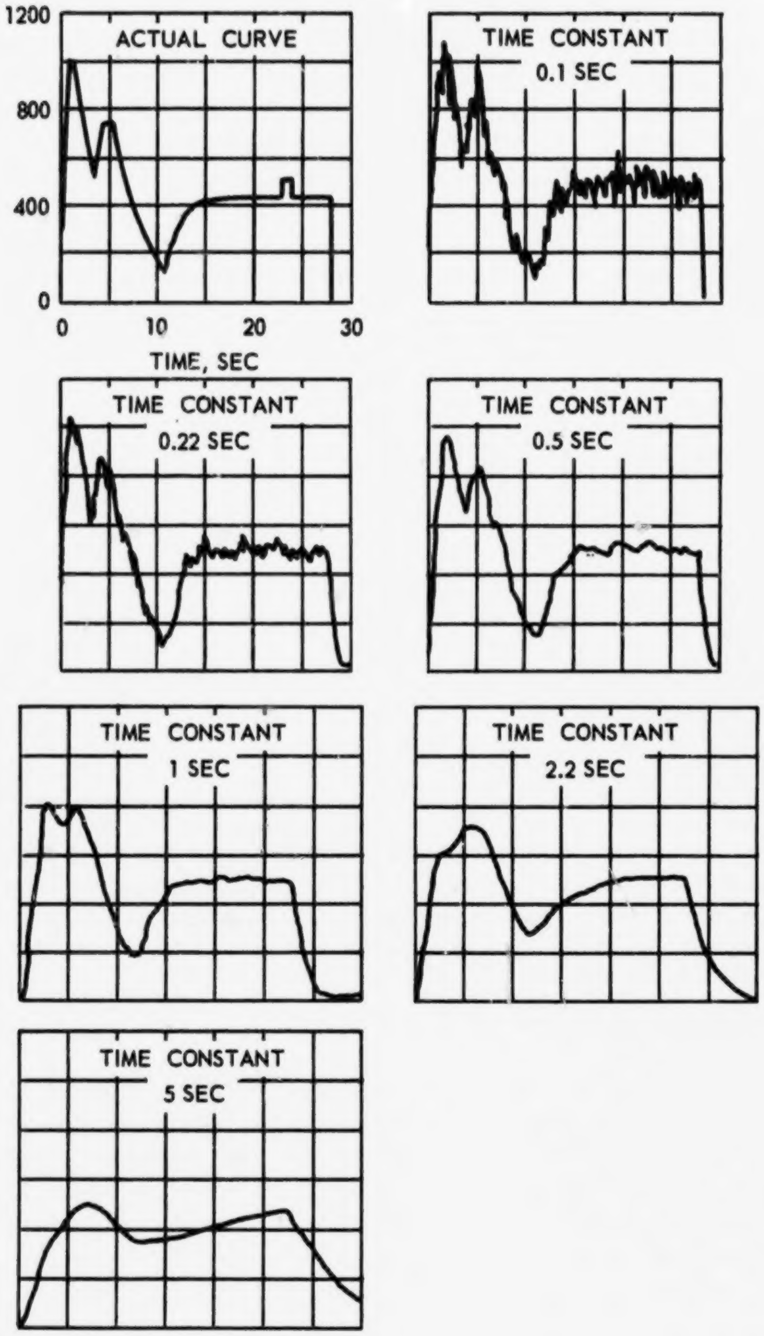

Figure XII-2.--Mock Cardiac Output Patterns

(USAEC/DTI TID-7678)

Figure XII-2 shows a mock cardiac output pattern compared with analog ratemeter recorder curves at various time constants. This example clearly demonstrates the distortion which results from using a too long time constant. As the time constant is increased, the peaks are depressed, and the valleys are elevated. Hence, the curve approaches a horizontal line as would be expected for longer and longer averaging times.

b. Digital ratemeter with high-speed recorder

In recent years, ratemeters have been developed that integrate counts digitally over a preselected time interval. These counts are divided by the integrating time to obtain a count rate. The integrating time can be made very short (down to 0.01 seconds), and the time required to average counts and display the information is negligible compared to the integrating time. The digital ratemeter emits a voltage signal at the end of each integrating interval, proportional to the average counting rate over that interval. This signal may be used to drive a high-speed recorder. The result is a histogram rather than a continuous curve. The advantage of the digital ratemeter over the analog is that the maximum time lag between the true change in counting rate and the ratemeter response is independent of the frequency of the change.

c. Other

Other devices have been developed in attempts to reduce the effect of the RC time-constant associated with analog ratemeters. These are digital in nature, and include devices to measure the time needed to collect a specified number of counts, as well as "multiscalar" devices on multichannel analyzers. The multiscalar consists of a "dwell" mode on a multichannel analyzer. This causes all photopeak pulses to be recorded in channel No. 1 for the first time interval, channel No. 2 for the second, etc. In other words, the channels on a 400 channel analyzer represent equal time intervals rather than energy increments. The time interval per channel can be made as short as one millisecond, or as long as several seconds.

IV. WHOLE-BODY COUNTING

The primary purpose of whole-body counting is to measure low levels of radioactivity in a human body. Although whole-body counting has been primarily a research and bioassay tool, much of the information obtained is finding clinical application.

The most difficult factors to control in whole-body counting, as with distributive in vivo counting, are counting geometry and absorption by the patient. Obviously, patients vary tremendously in size, weight, and shape. In studies that require multiple measurements performed at different times, the redistribution of the material within a single patient causes changes in the counting geometry. Hence, precise phantom mock-ups are generally needed to obtain valid quantitative results.

Various instrument systems have been designed to minimize the effect of geometry variations on instrument response.

A. Single-Detector Systems

Most single-detector, whole-body counters have a large (8 or 9 inch diameter) NaI(Tl) crystal suspended at the center of an arc defined by the contour of the patient's body. Hence, most parts of the body are approximately equidistant from the center of the detector. The patient may sit or lie on his side with his body in the shape of an arc. The radius of the arc is usually between 1 and 1.5 meters.

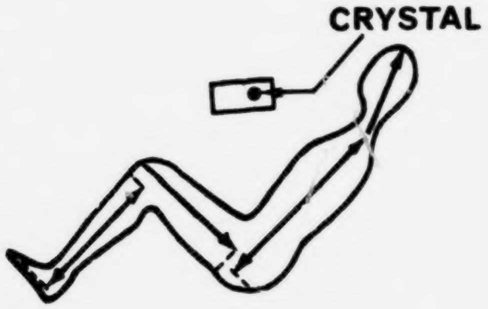

Figure XII-3.--Single Crystal Whole-Body Counter
Using Chair Geometry

B. Multiple-Detector Systems

Some whole-body counters use two, three, or four separate NaI(Tl) crystals. These are arranged so that their combined response to a point source is approximately independent of the position of the source along the line representing the longitudinal body axis of a person stationed under the crystals. These are referred to as multiple-crystal stretcher systems. Four-crystal stretcher systems (such as the one shown in Figure XII-4) can be made more geometry independent than can single detector systems.

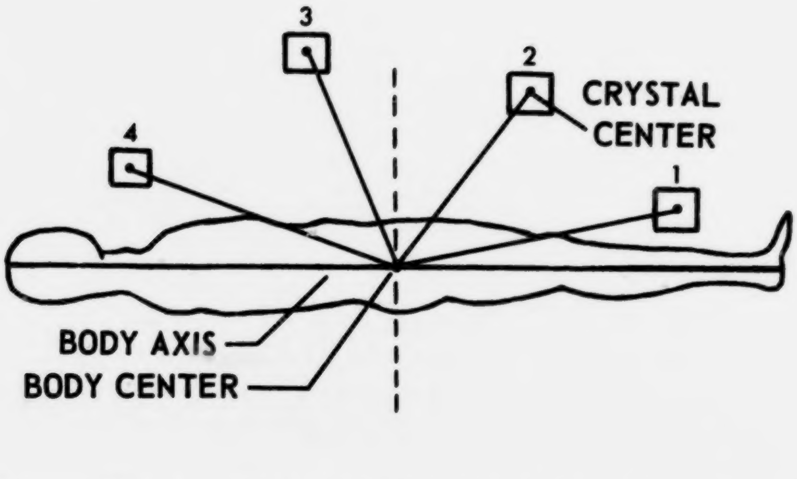

Figure XII-4.--Multiple Crystal Whole-Body Counter

C. Two-Pi and Four-Pi Systems

To further improve the counting geometry, large detectors may be positioned around the body in either a 2π or 4π (approximately) geometry. This way, most photons emitted from the body during a measurement are incident on the detector. Liquid and plastic scintillators are used in these systems. Although it is true that the geometry of such an arrangement is greatly enhanced over that obtainable with single or multiple NaI(Tl) crystals, the intrinsic efficiency (Chapter XI) of the low atomic number scintillators is much less, except for very low energy photons.

D. Moving Detector Systems

Single and multiple crystal systems may be used to obtain a "profile scan" of the patient, i.e., a measurement of the counting rate vs. position along the longitudinal body axis of the patient. Here, a slit collimator is generally combined with a large NaI(Tl) crystal. The scan is achieved by moving the crystal over the length of the patient at a constant speed, or the crystal may remain stationary. In the latter case, the patient is moved across the face of the crystal.

E. Sensitivity

The required sensitivity for whole-body counting depends on the radioactivity level in the patient. For relatively high activity levels, such as those administered in clinical diagnosis and therapy, no special shielding is required. For intermediate levels, a portable "shadow-type" shield around the detector may sufficiently reduce the background. However, accurate measurements for low levels of activity--such as the measurement of the naturally occurring ^{40}K in a person's body or the assessment of minute amounts of radionuclides in the body from occupational exposure--the entire assembly is generally enclosed in a shielded room. The walls of these rooms must be constructed of steel free of all fission product activity. Steel rooms for whole-body counters weigh as much as 65 to 70 tons. Such rooms can also be used for distributive counting applications.

F. Data Recording

Any of the counting systems described in Chapters VII and VIII can be used with whole-body counters. However, in permanent installations where large volumes of data are accumulated, the instrument of choice is usually the multichannel analyzer. Many installations transfer the whole-body counting data from the multichannel analyzer to magnetic tape or paper punch tape for computer analysis.

SUGGESTIONS FOR FURTHER READING

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2. Hine, G. J., Instrumentation in Nuclear Medicine, Academic Press, Inc. (1967), chaps. 14 and 15.

3. Wagner, H. N., Principles of Nuclear Medicine, W. B. Saunders Co. (1968), pp. 130-138.

CHAPTER XIII

UNITS OF RADIATION EXPOSURE AND DOSE

I. INTRODUCTION

Fundamentally, the harmful consequences of ionizing radiation to a living organism are due to the energy absorbed by the cells and tissues. This absorbed energy (or dose) produces chemical decomposition of the molecules present in the living cells. The mechanism of the decomposition appears to be related to ionization and excitation interactions between the radiation and atoms within the tissue. The amount of ionization or number of ion pairs produced by ionizing radiations in the cells or tissues provides some measure of the amount of decomposition or physiological damage that might be expected from a given quantity or dose. The ideal basis for radiation dose measurement would be, therefore, the number of ion pairs (or ionizations) taking place within the medium of interest. For certain practical reasons, the medium chosen for defining exposure is air.

II. EXPOSURE--THE ROENTGEN

The exposure of x or gamma radiation within a specific volume of air is a measure of the amount of radiation, based on its ability to produce ionization in air. The unit that expresses x or gamma radiation exposure is the roentgen (R). Its merit lies in the fact that the magnitude of the exposure in roentgens can usually be related to the absorbed dose, which is important in predicting or quantitating the expected biological effect (or injury) resulting from the radiation.

The roentgen has been defined as an "exposure of x or gamma radiation such that the associated corpuscular emission per 0.001293 gram[1] of air produces, in air, ions carrying one electrostatic unit of quantity of electricity of either sign." Since the ionizing property of radiation provides the basis for several types of detection instruments, such devices may be used to quantitate the exposure. It is emphasized that the roentgen is a unit of exposure based on ionization of air; it is not a unit of ionization, nor is it an absorbed dose in air.

III. ABSORBED DOSE--THE RAD

The absorbed dose from any ionizing radiation is the energy imparted to matter (irradiated material) by that radiation per unit mass of material at the place of interest. The unit of absorbed dose is the rad. One rad is equivalent to the absorption of 100 ergs/gram of absorbing material. Although the roentgen unit is strictly applicable only to x or gamma radiation, the rad unit may be applied regardless of the type of ionizing radiation or the type of absorbing medium.

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[1] The weight of 1 cc of air at standard conditions of temperature and pressure.

The following example will illustrate how the exposure may be related to the energy absorbed, or the absorbed dose:

A radiation detection instrument was used to measure the exposure from a gamma source at some point in air. The exposure measured was one roentgen. How much energy was absorbed per gram of air at the irradiated point? (Assume standard conditions of temperature and pressure.)

To form 1 electrostatic unit per 0.001293 gram of air, the radiation must produce 1.61×10^{12} ion pairs when absorbed in 1 gram of air. It is known that, on the average, 34 electron volts of energy are transferred (or absorbed) in the process of forming each ion pair in air. Thus, the total energy absorbed is:

$$\frac{34\ \text{eV}}{\text{ion pair}} \times 1.61 \times 10^{12}\ \frac{\text{ion pairs}}{\text{gram}} = 5.48 \times 10^{13}\ \text{eV/gram}$$

or, expressed in ergs rather than electron volts:

$$5.48 \times 10^{13}\ \frac{\text{eV}}{\text{gram}} \times 1.602 \times 10^{-12}\ \frac{\text{erg}}{\text{eV}} = 87\ \text{ergs/gram}$$

Since 100 ergs/gram is 1 rad, then one roentgen of exposure to a specific volume of air at standard conditions results in the absorbed dose of 0.87 rad.

IV. RELATIVE BIOLOGICAL EFFECTIVENESS AND QUALITY FACTOR

Although all ionizing radiations can produce similar biological effects, the absorbed dose, measured in rads, that will produce a certain effect may vary appreciably from one type of radiation to another. The difference in behavior, in this connection, is expressed as a quantity called the "relative biological effectiveness" (or RBE) of the particular nuclear radiation. The RBE of a given radiation may be defined as the ratio of the absorbed dose (rads) of gamma radiation (specified energy) to the absorbed dose of the given radiation required to produce the same biological effect. Thus, if an absorbed dose of 0.2 rad of slow neutron radiation produces the same biological effect as an absorbed dose of 1 rad of gamma radiation, the RBE for slow neutrons would be:

$$\text{RBE} = \frac{1\ \text{rad}}{0.2\ \text{rad}} = 5$$

The value of the RBE for a particular type of nuclear radiation depends on several factors: energy of radiation, kind and degreee of biological damage, and nature of the organisms or tissue under consideration. Hence, for radiation protection work, a more general term is the "quality factor." The quality factor is an average RBE factor based on macroscopic effects of radiation on the human organism. The quality factor is now used in setting radiation protection standards. The term RBE is reserved for radiobiological work which demands more precise values. Typical values of the quality factor for several types of radiation are given in Table 1.

TABLE XIII-1.--Quality Factors (QF) for Radiation of Different Types

Radiation	QF
x or gamma	1
beta	1
proton	10
alpha	10
fast neutron	10
slow neutron	5

V. REM AND DOSE EQUIVALENT

With the concept of the RBE or quality factor in mind, it is now useful to introduce another unit, the "rem," an abbreviation of "roentgen equivalent man."

The rad is a convenient unit for expressing energy absorption, but it does not take into account the biological effect of the particular nuclear radiation absorbed. The rem, however, does:

$$\text{dose in rems} = \text{RBE} \times \text{dose in rads.}$$

This provides an indication of the extent of biological injury (of a given type) that would result from the absorption of nuclear radiation. Again, for purposes of radiation protection work, a different unit is employed, the dose equivalent. The dose equivalent is equal to the product of the absorbed dose in rads and the quality factor. The rem and dose equivalent are units of biological dose.

As Table XIII-1 shows, the quality factor for gamma rays is approximately unity. In general, the gamma radiation dose equivalent for humans is numerically equal to the absorbed dose in rads; it is also roughly equal to the exposure in roentgens.

VI. RADIATION PROTECTION GUIDES (RPG)

Three independent organizations have issued recommendations governing the exposure of persons occupationally exposed to ionizing radiation. These are the National Committee on Radiation Protection (NCRP), the International Commission on Radiological Protection (ICRP), and the Federal Radiation Council (FRC).

The following table gives the current recommendations for persons occupationally exposed. The values should be regarded as upper limits, not to be exceeded without good reason for doing so.

Organs	RPG*
gonads, red bone marrow, whole body	5 rems/yr
skin, thyroid, and bone	30 rems/yr
hands and forearms	75 rems/yr
all other organs	15 rems/yr

*One half the annual RPG is permitted within a period of 3 months.

VII. CORRELATION OF UNITS OF EXPOSURE AND ACTIVITY

The following expression relates the exposure rate in milliroentgens per hour at a given distance from a point source to the activity of the source in millicuries:

$$I_\gamma = (1.56 \times 10^4) \sum_i E_i \times n_i \times \mu_{ai}$$

Where:

I_γ = mR/hr at one meter per millicurie of activity

E = gamma energy in MeV

n = number of photons of energy, E, per disintegration

μ_a = linear absorption coefficient for photons of energy E in air (units - cm^{-1})

Example: Sodium-24 emits two gamma photons per disintegration. Their energies are 1.38 MeV and 2.76 MeV respectively. The μ_a in air for the 1.38 MeV photons is 3.1×10^{-5} cm^{-1}. Thus, $I_\gamma = 1.56 \times 10^4 \, [(1.38)\,(1)\,(3.1 \times 10^{-5}) + (2.76)\,(1)\,(2.65 \times 10^{-5})]$ or, $I_\gamma = 1.8$ mR/hr per millicurie at 1 meter. Exposure rates at other distances are determined using the inverse square law. (See Chapter V.)

SUGGESTIONS FOR FURTHER READING

1. NBS Handbook 84, "Radiation Quantities and Units," International Commission on Radiological Units and Measurements, Report 10a (1962).

2. International Commission on Radiological Protection, ICRP Pub. 9, Pergamon Press, Inc., New York (1966).

CHAPTER XIV

RADIATION PROTECTION INSTRUMENTATION

I. SURVEY INSTRUMENTS[1]

Survey instruments are used to measure external radiation levels in areas where radioisotopes are stored and used and to monitor for contamination in the laboratory. Survey meters are similar to other radiation instruments in their operational characteristics. A survey meter should be portable, rugged, sensitive, simple in construction, and reliable. Portability implies lightness and compactness with a suitable handle or strap for carrying, and generally a self-contained power supply. Ruggedness requires that an instrument be capable of withstanding mild shock without damage, and sensitivity demands response to the type and energy of radiation being measured. Rarely is one instrument capable of measuring all types and energies of radiation that are encountered in practice. Simplicity in construction necessitates convenient arrangement of components and simple circuitry comprised of parts which may be replaced easily. Reliability is that attribute which implies the ability to duplicate response under similar circumstances. Reliability may be determined by checking the response to a suitable standard source periodically. Although all of these conditions may not be met in any one instrument, they are approached in many. In any monitoring situation, one must select the proper instrument, use it intelligently, and then be able to interpret the results of the meter readings.

A. Energy Dependence

The phenomenon known as energy dependence is one which is inherent in all normal roentgen measuring survey instruments. If a survey meter is said to be "energy dependent," or has "poor energy dependence characteristics," it means that its readings are not only dependent upon intensity but also upon the energy of the radiation being measured.

There are basically two reasons for energy dependence in survey meters designed to measure radiation in terms of the unit known as the roentgen. (The roentgen is a measure of the potential ability of x or gamma radiation to produce a specific amount of ionization in air.)

Because the ions collected within a typical ionization chamber are produced in the chamber walls, it is imperative (from the definition of the roentgen) that the walls be made of an air-equivalent material. The thickness of the chamber walls is also of concern because the probability of interaction and the penetrating ability of x and gamma rays, as well as their associated corpuscular emissions, are functions of energy. Very high or very low energy radiation will lower chamber response. Ideally, the thickness of the chamber walls should be adjustable to suit the energy of the radiation. However, this is not done in practice and the response of a given chamber will not be the same for all energies of radiation.

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[1] The student may wish to reread Chapter VI in order to refresh his memory of the basic principles of radiation detection before reading this chapter.

B. Ionization Chambers

1. Characteristics.

Ionization chambers are instruments in which the ionization produced within the chamber by radiation is measured without further gas-amplification. (Chapter VI.) Primary ions formed in the chamber are attracted to the respective electrodes, and the current pulses are amplified externally to a measurable current. The gas amplification factor is thus unity. Because air-filled ionization chambers with air-equivalent walls collect only the primary ions associated with the radiation being monitored, they are basically well adapted to measure roentgens. Often they are referred to as being "fundamental" exposure measuring instruments in that their design is based upon the definition of the roentgen.

2. Operation

Most ionization chamber survey instruments have a selector switch marked "off", "wait," and X1, X10, X100. When the switch is off, the batteries are disconnected and the meter is short-circuited making the instrument inoperative. With the switch in the wait position, the batteries are connected, permitting the circuit to warm up and the instrument to be zeroed after a warm-up period of from 1 - 5 minutes. Some instruments have a zero position in which the meter is connected while the ionization chamber is disconnected, making it possible to adjust the meter to zero even in the presence of radiation.

The ionization chamber does not wear out or suffer changes in characteristics as G-M tubes do; however, the circuit of the ionization chamber survey meter has many elements which can go out of adjustment if not properly handled. Loose leads and weak batteries are sources of trouble, but can be readily serviced. Other difficulties are usually caused by faulty circuits which cannot generally be fixed without the aid of a competent service man.

3. Uses

Ion chambers perhaps find their best use as roentgen measuring instruments. However, certain ones are also used for alpha and beta monitoring and, when properly modified, may be used for high energy particle accelerator survey and neutron monitoring. In general, ion chambers have low sensitivity and high range. They can be designed to have relatively high precision and good energy dependence characteristics, and are desirable instruments for general radiation safety and survey work.

4. Typical instruments

a. Condenser R-meters

The condenser R-meter is a very reliable and accurate instrument for measuring exposures of x and gamma rays. It has excellent energy dependence characteristics and because of its great precision is often used as a secondary standard. The condenser R-meter measures cumulative exposure and consists of a charger-reader mechanism and several detachable ion chambers. The chambers are available in ranges from .025 roentgens full scale to 250 roentgens full scale and are designed for photon energy ranges as follows:

low energy - 6 to 50 keV
medium energy - 50 to 400 keV
high energy - 400 to 1,300 keV

Rated accuracy, which is dependent upon chamber size and energy range design, varies from ± 2% to ± 10%, provided the chamber is used in its proper energy range.

b. "Cutie pie"

The "cutie pie" is perhaps one of the most widely used instruments available for radiological survey work. It measures exposure rate. Typical full scale ranges are: 0.005, 0.05, 5, and 50 R/hr. In general, cutie pies are intended to measure only x and gamma radiation though some have thin "end-windows" which also allow beta particles to enter the chamber. Most cutie pies are air filled, have relatively high range and low sensitivity, and are designed to have good energy dependence characteristics.

c. Miscellaneous ion chambers

There are other ionization chambers which are fairly unique in their design or operational characteristics. One of these is an alpha monitor called the Samson; it has a large thin Mylar window which alpha particles are able to penetrate. Another instrument called the Juno has movable shields which allow discrimination between alpha and beta - gamma radiation. A third type of ion chamber, called the Radgun, is designed for beta and gamma monitoring. It is constructed of steel and is filled under high pressure with pure argon gas. A three decade logarithmic meter and a three range selector switch together make possible a range of 0.01 mR/hr to 10,000 R/hr. The logarithmic ratemeter on the Radgun exhibits extremely slow time response.

C. Geiger Mueller (G-M) Instruments

1. Characteristics

Since one measures each beta particle and each gamma ray that produces ionization within the sensitive tube volume, the G-M instrument is extremely sensitive to radiation. On the most sensitive scale background radiation levels can be read.

A discriminating shield is provided for the G-M tube or probe which when open admits both beta and gamma. With the shield closed only gamma radiation is admitted.

The indicating mechanisms on Geiger counters are usually two-fold, viz., earphones for audible response and a microammeter for visual indication. In general, the dial of the meter is calibrated in counts/minute and/or milliroentgens/hour. The instrument also has a switch for selecting different ranges of sensitivity.

2. Operation

The operation of the G-M survey instrument is essentially the same as that of the ionization chamber survey instrument. The warm-up period is much less critical, and usually 5 to 10 seconds is ample. Care should be taken not to exceed the maximum capacity of the instrument; such excessive exposure may damage the G-M tube. The G-M tube is in operation when in the "on" position and no zero adjustment is possible. It is important to remember that G-M survey meters are sensitive instruments and in general do not read high levels of radiation intensity. Furthermore, many G-M counters when exposed to radiation intensities beyond their capacity, will "swamp"; i.e., fall back from full scale and give a low, but deceptively "real" reading.

Because G-M counters normally do not have air equivalent walls and are essentially count ratemeters, rather than primary ionization measuring devices, they tend to be very energy dependent. When used to measure x or gamma radiation in units of roentgens, they must be calibrated with known quantities of radiation of the appropriate energy range.

D. Uses

Geiger-Mueller survey instruments are useful for low-level beta and gamma survey work. Their high sensitivity makes them very desirable for monitoring contamination and for detecting lost sources. In this respect earphones are especially desirable, because the surveyor does not have to continually look at the meter to get a response. Full scale ranges in a typical G-M survey meter are: 0.2, 2.0, and 20 mR/hr.

E. Proportional Survey Instruments

1. Characteristics

Proportional instruments are named after the region of the instrument response in which they operate. (Chapter VI). Survey instruments of this type use a probe which has an extremely thin window which admits alpha particles into the chamber. The operating voltage is typically of the order of 1,500 to 4,000 volts, with gas amplification factors of 10^5 to 10^6. The voltage stability requirement for proportional counters is much greater than for G-M counters. The main advantage of instruments which operate in the proportional region rather than the G-M region is their inherent capability of distinguishing alpha from beta and gamma radiation. Alpha particles, because of their high specific ionization, produce larger pulses than do beta particles and gamma rays. By proper voltage selection and discriminator adjustment, it is possible to discriminate against the smaller beta and gamma pulses while accepting and reading those due to alpha particles.

The meter is usually marked in counts per minute with several sensitivity scales. Earphones can also be used with proportional counters.

2. Operation and uses

The operation of the proportional radiation survey instruments is similar to other instruments. A warm-up period of several minutes is usually required to allow the circuit to become properly stabilized.

By reason of their inherent capability of discriminating between alpha and beta-gamma radiation, proportional survey instruments are very desirable as alpha contamination monitors.

F. Scintillation Survey Instruments

1. Characteristics

Scintillation phosphors may be liquid or solid, but for survey work the solid type is, at present, preferable. To detect alpha radiation, a thin layer of silver-activated zinc sulfide is generally used. For the detection of beta radiation, phosphors such as naphthalene, stilbene, or anthracene are used. These are covered with a thin metal foil to shield against alpha radiation. Sodium iodide crystals sealed in a housing which will shield against alpha and beta particles are used for gamma radiation detection.

2. Operation and uses

Operation of scintillation survey instruments is similar to that of ion chambers and G-M instruments. It should be pointed out that the photomultiplier tube of a scintillation instrument may be damaged if exposed to light without first removing the voltage applied to the tube.

As previously pointed out, scintillation devices may be used to detect either alpha, beta, or gamma rays depending upon the phosphor used. Scintillation survey instruments are even more sensitive and efficient than G-M counters, particularly to gamma radiation, and may be used to detect extremely low levels of activity. Losses due to dead time in a scintillator are very slight, as the decay time of the light flash is very short.

At present, scintillators find their greatest use as alpha, gamma and neutron radiation monitors. However, they, as well as proportional counters, tend to be considerably more expensive than either ionization chambers or G-M survey instruments.

C. Calibration of Survey Instruments

The meters on some survey instruments are calibrated to read directly in units of radiation activity or intensity such as: disintegrations per minute, mR per hour, or neutrons per square centimeter per second. However, this may lead to considerable error because changes in the characteristics of individual components of the instrument from the time of the manufacturer's calibration may cause a change in instrument response. Also if measurement of a different type or energy of radiation than that used by the manufacturer is made, the results may be in error. It is essential that all survey meters, whether they are direct reading or relative reading devices, be calibrated periodically to ensure proper reading.

Survey instruments should be calibrated under the same conditions for which they are intended, and with known intensities of radiation of the same type and energy as the radiation to be monitored. It is important to calibrate the meter over the entire scale on each range selector setting to determine any dose rate dependence.

II. PERSONAL MONITORING INSTRUMENTS

Personal monitoring instruments are designed to measure the accumulated external exposure or dose a person receives over some time interval. Hence, they are integrating devices rather than dose rate meters as are many survey instruments. This means they must be light and compact enough to be carried on the person during all working hours. Also, they must be relatively inexpensive because each person in the laboratory who works with radioactivity must wear some type of personal monitoring instrument.

The ideal personal monitoring instrument would accurately measure the biological dose in rems received by those parts of the body considered to be most vital from the standpoint of chronic, low level radiation exposures, i.e., blood forming organs and reproductive organs. This ideal instrument would also give an accurate measurement of dose independent of the type and energy of the radiation producing the dose. Since these criteria are not met in any instrument presently available, it is necessary to start with a conveniently measured quantity. For x and gamma radiation, the roentgen can be readily measured in air at the surface of the body. Then, the biological dose to organs at different depths within the body may be estimated by means of calculations which are beyond the scope of this manual. Personal monitoring instruments that measure the roentgen are: photographic film, self-reading pocket dosimeters, and condenser type pocket chambers. In recent years, thermoluminescent media have been used in personal dosimeters. This type of device measures energy absorption directly and the reading can be readily measured in air at the surface of the body. This type of device measures energy absorption directly and the reading can be readily converted to rads.

A. Film Dosimetry

The most widely used personal dosimeter at present is the film badge which consists of one or more small sheets of photographic film enclosed in a plastic packet. Film dosimetry offers three important advantages:

(1) It provides a permanent record of each individual's accumulated exposure.

(2) It is economical: costs range from less than 50 cents to $1.50 per reading, depending on the number of films read.

(3) No technical knowledge of dosimetry is required of the user.

When radiation is absorbed in a film emulsion, some of the silver halide grains which make up the emulsion are altered in such a way that they react differently toward certain reducing agents known as developers, i.e., those grains affected by the radiation are reduced to metallic silver by the developer at a faster rate than the other grains which were not affected. This developable state produced in a photographic grain by the action of the radiation is called the latent image. The optical density of the developed film is proportional to the exposure in roentgens. The exposure vs. density relationship must be determined by a comparison with films exposed to known amounts of radiation of the same energy since the optical density produced by a given exposure of radiation is strongly dependent on the energy of the radiation. Photographic emulsions are much more sensitive to low energy radiation than to high energy. Many film badges include metallic filters which attenuate the low energy radiation in varying degrees, thereby enabling the reader to estimate the energy of the radiation to which the film was exposed.

Photographic film may also be used to monitor external beta radiation doses, although, as stated previously, the roentgen unit does not apply.

In most laboratories, films are changed once each month. Longer accumulating periods would be possible were it not for the fact that the latent image may fade appreciably after long periods of time.

B. Self-Reading Pocket Dosimeter

A self-reading pocket dosimeter is a chamber containing two electrodes, one of which is a quartz fiber loop, free to move with respect to its mounting. Like charges from an external voltage source are placed on the loop and its mounting resulting in a repulsive force between the two which forces the loop outward from the mount. Ionization in the chamber reduces the charge and allows the fiber to move toward its normal position. An optical system and a transparent scale are all enclosed in the instrument, which is about the size and shape of a large fountain pen. The end of the dosimeter opposite the eyepiece is made of glass to allow light to enter. Hence, the quartz fiber casts a shadow on the transparent scale, which is calibrated in milliroentgens or roentgens. The advantage of the self-reading pocket dosimeter is that it can be read at any time without the aid of a supplementary reader simply by holding it up to a light source and looking into it.

C. Condenser Type Pocket Chamber

A condenser type pocket chamber has a cylindrical electrode well insulated from a Bakelite wall. A charge is placed on the center electrode by means of an external charging unit. Ions formed in the chamber reduce the charge by an amount proportional to the radiation exposure. The condenser type pocket chamber differs from the self-reading dosimeter mainly in that the quartz fiber mechanism and optical system are in an external unit. Hence, the chamber must be read with a separate unit called a charger reader. The pocket chamber is similar in size and shape to a fountain pen. The advantage of this unit is its low cost as compared to a self-reading dosimeter. Both types of dosimeters should be recharged daily since significant leakage of charge may occur over long periods of time.

D. Thermoluminescent Dosimeter

Thermoluminescent dosimeters are small vials containing a small amount of some thermoluminescent powder such as lithium flouride. Upon exposure to ionizing radiation, electrons in the crystalline structure of the material are excited to higher energy states where a certain number are "trapped" in "sensitivity centers" (see Chapter VI). Upon heating of the powder, the electrons return to the ground state and the excitation energy appears in the form of visible light. The intensity of the light is proportional to the energy absorbed by the crystal. Advantages of thermoluminescent dosimetry are: (1) it provides a direct measurement of energy absorption, (2) the powder can be reused indefinitely as long as it is properly heated ("annealed") after each exposure, and (3) dosimeters can be used for several weeks at a time without appreciable loss of the stored energy.

III. SUMMARY

Radiation protection instruments as used in nuclear medicine laboratories fall into two categories - survey instruments and personal monitoring instruments. Survey instruments are used to ascertain the external radiation levels which exist in areas where personnel or the general public may be exposed and to check for radioactive contamination. G-M tubes, ionization chambers, and scintillators are commonly used in survey instruments. Personal monitoring instruments are used to measure the amount of radiation dose received by laboratory personnel. Types of personal monitoring instruments include film badges, self-reading pocket dosimeters, condenser type pocket chambers, and thermoluminescent dosimeters.

CHAPTER XV

PRINCIPLES OF RADIATION PROTECTION

I. INTRODUCTION

To facilitate the discussion of radiation protection, sources of radiation exposure can be divided into two categories: external and internal. Sources of external exposure are outside the body, e.g., x-ray machines, sealed and unsealed sources of radioactive materials, etc. Internal exposure sources are radioactive materials that gain entrance into the body through ingestion, injection, inhalation, or absorption through the skin.

II. EXTERNAL RADIATION HAZARDS

A. Sources

Gamma rays from radioisotopes are the most common external radiation hazard encountered in nuclear medicine laboratories. Because of their high penetrating power, high energy gamma rays can irradiate the entire body almost uniformly. Low energy gamma rays and x rays are less penetrating, and result in a more superficial dose distribution.

Under certain circumstances, beta particles may constitute an external radiation hazard. The dose from the beta particles themselves is limited mainly to the skin. However, enough bremsstrahlung interactions (see Chapter V) in the source container may turn a "pure" beta emitting source into an x-ray generator. Hence, the nature of the external hazard associated with beta particles is twofold.

Neutrons are a very significant external radiation hazard. The nuclei set in motion by collision with neutrons have extremely high values of specific ionization, causing a high relative biological effectiveness with neutron irradiation. But most nuclear medical technologists are not exposed to neutron sources. High levels of external neutron radiation are limited primarily to nuclear reactors and particle accelerator installations. Therefore, neutron protection principles are not discussed here.

Alpha particles from radionuclides constitute no external radiation hazard, because even the most energetic ones will not penetrate the horny layer of the epidermis.

B. Principles of Protection

1. Distance

Distance is not only very effective but, in many instances, is the most easily applied principle of radiation protection. Beta particles of a single energy have a finite range in air. Sometimes the distance afforded by the use of remote control handling devices will supply complete protection. The inverse square law for reduction of radiation intensity applies for point sources of x and gamma radiation.

The inverse square law states that radiation intensity from a point source varies inversely as the square of the distance from the source. Expressed mathematically,

$$\frac{I_1}{I_2} = \frac{(R_2)^2}{(R_1)^2}$$

Where: I_1 = radiation intensity at distance R_1 from the source

I_2 = radiation intensity at distance R_2 from the source

Inspection of this formula will show that doubling the distance from the source decreases the intensity by a factor of 4; increasing the distance by a factor of 3 reduces the radiation intensity to $\frac{1}{9}$ of its value, etc. The inverse square law does not apply to extended sources or radiation fields arising from multiple sources.

X-ray tubes act sufficiently like point sources so reduction calculations by the inverse square law are valid. Gamma-ray sources whose dimensions are small in comparison to the distances involved may also be considered point sources.

2. Shielding

Shielding is another prime principle of radiation protection. To apply shielding methods to x-and-gamma sources, one must understand how x and gamma radiation are attenuated in an absorbing medium. Energy is lost by three principal methods--photoelectric effect, Compton effect, and pair production.

The predominant mechanism depends on the energy of the radiation and the absorbing material. The photoelectric effect is most important at low energies, the Compton effect at intermediate energies, and pair production at high energies. The last cannot occur unless the incident radiation has at least 1.02 MeV of energy. As x- and gamma-ray photons travel through an absorber, the amount of attenuation is governed by the energy of the radiation and the type and thickness of the absorbing medium. Mathematically, this may be expressed as

$$I = I_0 e^{-\mu_0 x}$$

where: I_0 = intensity of radiation beam at point P with no absorber present

I = intensity of transmitted beam

μ_0 = linear attenuation coefficient

x = thickness of absorber

e = base of natural logarithms

The relation is shown diagrammatically in Figure XVI-1.

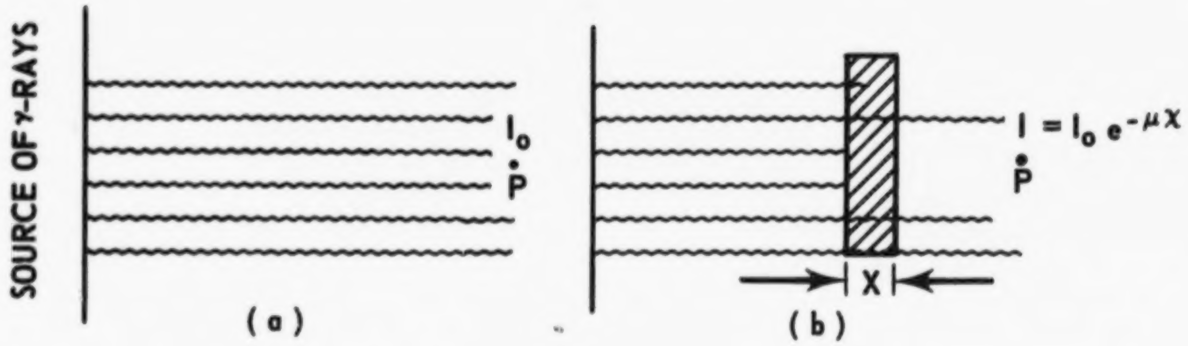

Figure XVI-1.--Radiation Intensity
(a) No absorber and (b) Absorber

Using this formula, one can calculate the radiation intensity behind a shield of thickness x, or calculate the thickness of absorber necessary to reduce the radiation intensity to a desired level as long as the factor μ is known. This factor is called the linear attenuation coefficient. The value of μ_0 however, depends on the energy of the radiation and the type of absorbing medium.

Tables and graphs are available that give values of μ_0 determined experimentally for all radiation energies and for many absorbing materials. The larger the value of μ_0, the greater the reduction in intensity for a given thickness of material. The fact that lead has a high μ_0 for x and gamma radiation is partially responsible for its wide use as a shielding material.

The preceding equation is identical mathematically to the decay law (Chapter III), i.e., gamma-ray attenuation in matter basically follows an exponential relationship. The attenuation can depart from this simple exponential law if a significant amount of scattered radiation contributes to the intensity at the point of interest, i.e., the exponential equation assumes all interactions are total absorption events. The Compton effect results in only partial energy absorption. The scattered photons may significantly increase the radiation intensity over what would be predicted by the exponential equation. If this is the case, an empirically determined factor, called the buildup factor, is used to compensate for the scatter. The equation becomes $I = b_0 I_0 e^{-\mu_0 x}$, where b_0 is the buildup factor. Tables of buildup factors appear in several references.

When designing shields, it must be remembered that gamma rays can be scattered from walls, floors, and other structures near enough for scatter to be appreciable. A simple "shadow shield" may not always be adequate. It may be necessary to completely enclose high level gamma sources to reduce the radiation intensity in nearby areas to an acceptable working level.

Shielding will also attenuate beta radiation, and it takes relatively little shielding to absorb it completely. Therefore, the general practice is to use enough shielding for complete absorption. For low energy beta emitters in solution, the glass container generally gives complete absorption. In many cases, plastic shielding is effective and convenient. The absorption of high intensities of beta radiation results in the production of another electromagnetic radiation, bremsstrahlung. This is x radiation caused by the deceleration of the beta particles. It is more penetrating than the beta radiation that produced it, and must be considered in shielding calculations. Since bremsstrahlung production is proportional to the atomic number of the absorber, it can be minimized by using low Z materials for beta shielding. The same principles which apply to attenuating x and gamma radiation from conventional sources apply to shielding against bremsstrahlung radiation.

Tables or graphs are available that give the maximum range of beta particles of various energies in different absorbing mediums. These can be used to calculate the shielding necessary for protection against beta radiation.

3. Exposure time

It may occasionally be necessary to work in areas of high dose rates. This can be done safely by limiting the exposure time, so that the total dose received is within recommended limits. For example, the technologist working with a high level stock solution may have his hands exposed momentarily to high intensities of gamma radiation. However, by working expediently and efficiently, the exposure time can be limited to the point where the total dose to the hands is not excessive.

Some combination of the foregoing factors (time, distance, and shielding) can be used to limit the hazards involved in any procedure involving external radiation sources.

III. INTERNAL RADIATION HAZARDS

Internal radiation exposure results from the deposition of radioactive material within the body through inhalation, ingestion, or skin absorption. Internally deposited radioactive material produces continuous radiation exposure until it decays or is removed from the body by metabolic processes. Therefore, internal radiation exposure can be controlled only by preventing the entry of radioactive material into the body. It follows that internal exposure control is essentially a problem of contamination control.

The hazard created by a radionuclide inside the body depends on: (1) the amount of radionuclide in the organ; (2) the energy of the emitted radiation; (3) relative biological effectiveness (RBE) of the radiation; (4) uniformity of distribution within the critical organ; (5) size and essentiality of the organ; and (6) effective half-life of the radionuclide. The effective half-life of a radionuclide is a measure of the decrease in radioactivity in the tissue with time. It is determined by combining the radiological half-life (T_r) and biological half-life (T_b) as follows:

$$T_{eff} = \frac{T_b T_r}{T_b + T_r}$$

National Bureau of Standards Handbooks 48 and 42 group selected radionuclides according to their relative radiotoxicity by weighing the previously mentioned factors, considering the usual quantities involved and the modes of handling in typical experiments.

A. Type of material

1. Alpha emitters

Alpha particles lose their energy very rapidly in the medium through which they pass because of their relatively large mass and double positive charge. Their range is therefore very short. A 4 MeV alpha particle has a range in tissue of only a few hundredths of a millimeter and can travel only 3 cm in air. Accordingly, alpha particles do not present an external radiation hazard. However, alpha emitters do present one of the greatest internal hazards. When deposited throughout a vital organ, they can cause considerable damage because of their relatively high energies (4 to 9 MeV) and high specific ionization, and because their RBE factor in tissue is about 20 times greater than that for beta and gamma radiation. Also, many alpha emitting radionuclides concentrate in the compact bone, where metabolic turnover rates are very low. Alpha emitters, which have a long radiological half-life, can cause irradiation of bone tissue for many years after intake. Alpha emitters are not used in nuclear medicine procedures for the reasons just stated.

2. Beta emitters

Beta particles are lighter and have less charge than alpha particles. This results in a longer path of travel, with less specific ionization. Accordingly, the relative biological effect of beta particles is much less than that caused by alpha radiation. For example, the absorbed energy from beta radiation must be approximately 20 times greater (per unit mass of tissue) than that from alpha radiation to produce the same biological effect. Both alpha and beta emitting materials are considered primarily internal radiation hazards, although beta radiation may also represent an external hazard when the energy is sufficient to penetrate the dead layer of skin. External beta burns can be extremely painful and slow to heal.

Typical beta emitting nuclides include strontium-90, a fission product, which decays with a radiological half-life of 27.4 years. Its radioactive daughter, yttrium-90, is also a pure beta emitter. Strontium-90 has an effective half-life in the bone of approximately 17.5 years. It is a bone seeker and considered a very dangerous internal radiation source.

Iodine-131 is also a fission product and a beta-gamma emitter. It emits beta particles with average energies of 0.22 MeV. The effective half-life is about 7.6 days. The organ of highest concentration is the thyroid gland. National Bureau of Standards Handbook No. 48 classifies this radioisotope as "moderately dangerous." Because of its short half-life it would have to be ingested or inhaled in relatively large quantities or over a relatively long period to constitute a serious hazard.

3. Gamma emitters

Most alpha and beta emitters give off associated gamma radiation. Because of its relatively low specific ionization, less energy per unit path length is deposited in tissue from gamma photons than from particulate radiation of comparable energy. Hence, for materials that emit both particles and photons, the gamma rays are responsible for much less of the absorbed dose than the alpha and beta particles. Consequently, "pure" gamma emitters (i.e., no particulate radiation is emitted) represent much less of an internal hazard than do alpha and beta emitters.

B. Modes of Entry

1. Inhalation

For materials capable of being airborne (powders or volatile liquids), inhalation is one of the principal potential modes of entry into the body. The absorption, retention, and elimination of material taken in via the lungs depend on such parameters as particle size of the inhaled material, solubility, and rate of respiration of the individual.

2. Ingestion

Radionuclides can enter the body by absorption of ingested material from the gastrointestional (GI) tract. The per cent of ingested material absorbed by the bloodstream depends on its chemical and physical form. A large proportion of insoluble ingested material is rapidly excreted in the feces. However, irradiation of the GI tract itself by such materials may constitute a significant internal radiation hazard.

3. Absorption

Radioactive materials can also enter the bloodstream by absorption through the unbroken skin, or through abrasions, cuts, and punctures. Thus, all personnel working with radionuclides should follow proper procedures and wear protective clothing to prevent contact with the skin.

C. Fundamental Principles of Contamination Control

Internal radiation exposure can be controlled only by preventing the entry of radioactive material into the body. As previously stated, internal exposure control is essentially a problem of contamination control. The two fundamental principles of contamination control are containment and cleanliness.

The spread of radioactive contamination may be minimized at several points. Containment (i.e., the restriction of active materials to specified areas) is the first line of defense. This is achieved by adopting those operating techniques and laboratory methods best suited to the particular radionuclide, careful choice of equipment, and proper discipline.

1. Operating techniques

The choice of processes and techniques for handling radioactive materials is a very important part of contamination control. Important aspects to be considered are:

(1) During radiochemical operations, the working surface should be covered by either metal trays or a layer of disposable absorbent material to soak up spilled liquids. Blotting paper and diaper paper (heavy absorbent paper backed with impervious material such as oiled paper) are used extensively. The latter is preferable since it prevents liquids from reaching the bench top.

(2) It is worthwhile to carry out a complete "dummy run" on a new procedure with inactive materials before any manipulation involving radioactive sources is undertaken. In this way, unexpected difficulties may be discovered, weaknesses in equipment detected, and the procedure modified accordingly.

(3) Reliance should never be placed on single containers; suitable drip trays or double containers should always be used and should be capable of holding the entire contents of the primary containers.

(4) Potentially contaminated equipment should never be handled with bare hands, and pipettes must never be operated by mouth suction. Glass blowing in active areas or on contaminated equipment should be done with special techniques which avoid blowing by mouth.

2. Equipment

a. Radiochemical hoods

Laboratory operations accompanied by the evolution of radioactive fumes or gases require the use of radiochemical hoods. The inner surfaces of the hoods should be of nonporous material (e.g., stainless steel). The surfaces may also be covered with a strippable paint to permit easy decontamination.

b. Glove boxes

The glove box is a totally enclosed chamber in which alpha emitters and low energy beta sources can be handled safely. The advantage of glove boxes, apart from the obvious one of confining contamination within a totally enclosed space, is the small air supply compared to the generous air flow necessary in the usual hood system to prevent escape of activity into the working atmosphere. The disadvantages of glove boxes are the extra time and labor involved and the difficulties of working inside them, but they are indispensable for work with dry powders of highly toxic material above certain levels.

c. Segregation of equipment

All equipment used for handling the active material must be segregated and used only for this work. Marking the equipment "radioactive" helps. This segregation is particularly important for glassware and handling equipment such as tongs, which can easily transfer contamination from fume hoods to the open laboratory.

3. Discipline

a. Clothing

All personnel working in radiation areas must wear the prescribed protective clothing. The degree of clothing change considered necessary depends on the level of activity and the types of operations. In tracer laboratories, a standard laboratory coat will suffice. In intermediate level laboratories, laboratory coats and a change of shoes should be compulsory, and it may be necessary to have a complete change of clothing plus a shoe change. Associated facilities will range from coat-hooks in the laboratory to a suitably located change room.

b. Personal effects

Unessential personal items should not be taken into the active area. Food, drink, or smoking materials should remain outside an active area, and nothing should be placed in the mouth while working in an active area.

2. Cleanliness

Proper operating techniques must be supplemented by cleanliness and good housekeeping. These will minimize the spread of contamination and prevent the buildup of significant levels of contamination.

Cleanliness in a radioisotope laboratory goes beyond just visible cleanliness. It involves the regular monitoring of the laboratory equipment, personnel, and operating techniques, followed by prompt decontamination when necessary. Working surfaces, floors, and all other surfaces should be checked regularly.

In areas where no sources of sufficient strength to cause a high room background are stored, routine monitoring of bench surfaces, floors, etc., may be done with a portable survey instrument. The instrument must be one that will respond to the type and energy of the radiation used. (See Chapter XV.)

If a high background exists which would preclude the detection of traces of contamination with a survey instrument, small pieces of filter paper may be used to wipe the surfaces. These wipes may then be removed to another area and counted with a laboratory counter. Again, care must be taken to select a counter whose detector is sensitive to the type and energy of the radiation under study.

Everyone working in an active area should wash and monitor his hands before leaving, particularly at the end of the day and before eating.

D. Management of Spills

In the event of a "spill" or accident involving the contamination of an area, personnel protection and the immediate confinement of the contamination is of primary importance. A standardized approach should be well-known and followed when a spill occurs:

1. Confinement

Prevent spread of contamination by:

a. closing doors and windows

b. turning off fans, air conditioners, and other ventilation, if possible

c. closing ventilation ducts, if possible

d. vacating room leaving shoes and other garments at door

e. locking doors and, if airborne material is involved, sealing edges with tape.

Once the spill is thus confined, cleanup can be done later according to a well-constructed plan.

2. Decontamination

Work out a specific plan considering the physical facilities and the properties of the material spilled. Such a plan should include:

a. monitoring spill area to determine the extent of contamination and the hazard

b. making sure decontamination personnel have sufficient protective clothing

c. proceeding with decontamination by scrubbing surfaces with a detergent solution always working toward the center of the contaminated area, taking care not to spread the contamination to less active areas. Monitor frequently and thoroughly during the decontamination procedure. Monitor all personnel and materials before permitting their movement to clean areas.

IV. WASTE DISPOSAL

The radioactive waste material generated in nuclear medicine laboratories generally has low level radioactivity. By "low level" is meant that the wastes are of such low specific activity or of such low concentration that they may be disposed of directly by release to the air, water, or ground.

Disposal of liquid wastes into the sanitary sewerage system is permissible as long as the concentration of radioactivity is less than that which is considered safe for an adult to drink. Allowance may be made for other sewage discharged in the same building which will serve to dilute the radioactive waste. Often, solutions which are of too great a concentration to release at first can be diluted and released. If the half-life is short, they can also be allowed to decay until the concentration is below the acceptable level. The latter method requires a shielded storage space.

Most solid wastes from nuclear medicine laboratories can be incinerated with other refuse after an appropriate decay period. Some long-lived waste materials may need to be packaged and transported to designated burial sites for land burial. Some cities have commercial services for the collection of low-level wastes.

V. SUMMARY

The factors of time, distance, and shielding are used to reduce radiation exposures from external sources to acceptable levels. The control of contamination, use of proper equipment and protective devices, and good housekeeping practices will prevent excessive personnel exposure from internal sources.

SUGGESTIONS FOR FURTHER READING

1. Blatz, Hanson, Introduction to Radiological Health, McGraw-Hill Book Co. (1964), Chaps. 8 and 9.

2. Saenger, E. L., Medical Aspects of Radiation Accidents, USAEC (1963).

CHAPTER XVI

RADIOACTIVE TRACERS AND PHARMACEUTICALS

I. TRACER METHODOLOGY

The use of radioisotopes as a "tracer" has greatly facilitated the study of the anatomy and physiology of the human body. Tracers, in general, are materials used to label specific molecules, organisms, etc., thereby permitting the labeled entity to be followed in its physical movement or in the action of its metabolism. Radioactive tracers are used to study the kinetics of exchange, mixing, transport, turnover and removal of the labeled material. They are used to determine both qualitatively and quantitatively the *in vivo* distribution of the labeled material using methods described in previous chapters. Radioactive tracers are also used to determine and quantitate the *in vivo* distribution of a stable isotope of the same element, such as, the use of sodium-22 to measure exchangeable sodium. The basis for the latter application lies in the fact that, in general, the chemical properties of an atom depend upon the number and configuration of the orbital electrons and not on the energy states of the nucleus. Hence, a radioactive atom has the same chemical properties as the stable atoms of the same element. The radioactive isotope emits radiations which may be detected *in vivo* or *in vitro* making it useful as a tracer to study the behavior of that element or other materials onto which the radioisotope may be "tagged."

Compounds labeled with radioactive tracers used in diagnostic medicine are referred to as *radiopharmaceuticals*.

II. PROPERTIES OF RADIOISOTOPIC TRACERS

A. Physical Properties

1. Half-life

In order for a radioisotope to be useful in a particular study, its effective half-life in the organ or system of interest must be long enough to allow the desired information to be collected. For example, in the Schilling Test for vitamin B_{12} absorption, a tracer dose of vitamin B_{12} labeled with a radioisotope of cobalt is given the patient, and the urine is collected for 24 hours. The radioisotope in the urine is then counted to determine how much of the tracer dose was absorbed by the patient. One would not choose ^{61}Co for this application because it has a 1.65-hour half-life and would not be detectable after 24 hours unless a very high activity were administered. The isotope of choice is ^{57}Co which has a half-life of 267 days.

On the other hand, ideally, one would not use as a tracer a radioisotope with an excessively long half-life relative to the time required to complete a study. For this means that, unless the material is excreted rapidly, the patient will be receiving radiation exposure for some time after the useful information is obtained. Also, the longer the half-life, in general, the less the amount of the radioisotope which can be given the patient from patient dose considerations. This is particularly important in scanning applications where one of the factors limiting resolution is the rate of photon emission from the patient. Ideally, then, one uses a radioisotope with a half-life that results in a high count rate at the time the information is being recorded, and one that does not remain in the body for an excessively long time afterwards. For most scanning applications, with present equipment, the optimal half-life is of the order of a few hours.

2. Type and energy of emissions

Tracers used for in vivo studies must emit either gamma photons or x rays of sufficient energy to be detectable outside the body. Even the most energetic beta particles contribute nothing to the diagnostic information obtained in an in vivo counting application. They do, however, contribute significantly to the radiation dose to the patient. Hence, the ideal tracer for in vivo counting applications is one that emits a low to medium energy gamma ray with no particulate radiation. The energy of the gamma ray is important in scanning and other applications where collimation is required. Gamma rays with energies greater than 500 keV are difficult to collimate for localization purposes, whereas photon energies below 50 keV are absorbed to a high degree by soft tissue. Technetium-99m, which emits a 140 keV gamma ray with no particulate radiation and decays with a half-life of six hours, has the most desirable physical characteristics for in vivo applications of all the radioactive tracers yet developed.

B. Chemical Properties

1. Purity

Any impurities in a radiopharmaceutical must be identified and quantitated. Impurities may be other radionuclides such as radioactive daughter products or radionuclides produced as a result of nuclear reactions occurring within the material. If these radioactive impurities possess no chemical toxicity, they are not of consequence unless the type and energy of the radiation they emit interferes with the accurate measurement of the radiation from the primary radionuclide, or if their emissions result in an excessive radiation dose to the patient. If radionuclidic impurities are present in bothersome quantities, steps must be taken to remove them before the radiopharmaceutical can be used clinically. If the impurities have short half-lives compared to the primary radionuclide, a sufficient storage interval before use will solve the problem. If the half-life of the impurity is longer than that of the primary radionuclide, the problem is compounded because the percentage of the impurity increases with time. In this case, chemical separations may have to be performed to remove the impurity.

Nonradioactive impurities must also be delineated and the chemical toxicity of the compound and its metabolites must be known. These considerations, however, are not unique to radiopharmaceuticals and will not be discussed here.

C. Biological Localization

Of prime consideration in the development of radiopharmaceuticals for use in *in vivo* applications is the biological localization of the material in the body. This is especially true for imaging applications. Considerations of biological localization are particularly well presented in a paper by McAfee and Subramanian.[1] The student is urged to read this reference in its entirety. However, for those who may not be able to obtain the paper, selected portions are abstracted in the following material. The authors discuss the biological behavior of the elements according to their positions in the Periodic Table.

Group I

The monovalent alkali metal cations (Li, Na, K, Rb, and Cs) are freely ionized and do not form stable compounds in aqueous solution. They are readily absorbed from the gastrointestinal tract and excreted in the urine. Following injection, they are initially distributed almost uniformly in the soft tissues of the body. Within a few hours, the blood level falls, with deposition chiefly in muscle and large organs such as the liver and kidneys. At 4 days, from 10 to 50% of the injected radioactivity is contained in skeletal muscle. Sodium is eliminated twice as fast as the other members of the group, and there is a specific intracellular localization of potassium. The retention half-time in man increases progressively with the atomic number in this series. For Na the half-time is 11 to 14 days, whereas for Cs it is as long as 110 to 143 days. A small fraction is retained by the skeleton for prolonged periods (Rb 14%, Na 6%).

The "coinage metals" of Group IB of the Periodic Table, including Cu, Ag, and Au, have a completely different biological behavior than the Group IA alkaline metals. Cuprous ions concentrate in the liver and to a lesser extent in the kidney and spleen. A small amount is concentrated in bone. Excretion is largely through the kidneys. Silver ions readily combine with plasma proteins following injection, are rapidly removed by the liver, and are excreted through the bile into the feces. Salts of Au are relatively insoluble and therefore readily form colloids *in vivo*. The colloidal particles localize within the reticuloendothelial organs of the body (liver, spleen, and bone marrow) and are retained indefinitely. The nuclides ^{198}Au and ^{199}Au in colloidal form have been used for visualization of the liver in man. The positron emitter ^{64}Cu chelated with EDTA (ethylenediaminetetraacetate) has been employed for positron scanning of human brain tumors.

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[1] See reference 3 in "Suggestions for Further Reading."

Group II

Group IIA alkaline earth divalent cations (Be, Mg, Ca, Sr, Ba, and Ra) concentrate in the mineral phase of bone and are retained in the skeleton for long periods. They are absorbed from the gastrointestinal tract when administered orally, Ca more readily than the others of the group. The lightest member, Be, concentrates also in the liver and kidney and thereby tends to resemble the elements of Group IIB. In man, the distribution of Sr and Ca is similar during the first few days after intravenous injection. From 30 to 40% of the injected radioactivity is localized in the skeleton. Thereafter, preferential excretion of Sr over Ca takes place, through the kidneys. After 60 days, 60% of the Ca is retained in the skeleton and only 25% of Sr retained. Some excretion of Ca occurs in the feces. After the first few days, almost all of the retained radioactivity of these elements is contained in the skeleton. A small fraction is retained in the wall of the aorta. At a microscopic level, the concentration of these elements in bone is very nonuniform.

Because of the prolonged retention of these elements in the skeleton, only nuclides with a short physical half-life may be used in man. None of the nuclides of calcium are suitable for imaging purposes. The nuclides ^{85}Sr and ^{87m}Sr have been used for localization of skeletal abnormalities in man.

The Group IIB volatile nontransition metals (Zn, Cd, and Hg) are divalent cations whose inner orbitals are completely occupied with paired electrons. Chemically and biologically, they behave in a completely different fashion than the alkaline earth metals, and concentrate in the liver or kidney rather than in the skeleton. They are readily absorbed from the gastrointestinal tract when administered orally. Following injection, Zn attains its highest concentration in the liver (30 to 40% of the administered dose). There is also concentration in the prostate, with retention for long periods. A small fraction is retained in the skeleton and skin. Zinc is excreted predominantly in the feces. In man, the retention of Zn is even greater than in experimental animals, and the effective half-time for ^{65}Zn is greater than 100 days. The metabolic turnover rate of Zn is highly dependent on the amount of carrier present. Cadmium and Hg progressively accumulate in the kidneys, increasing in concentration for several days (to a maximum of 25% of the administered dose in rats). These ions are tightly bound to plasma proteins in the circulation, and on accumulation in the renal tubular cells of the renal cortex they probably become bound to sulfhydryl groups of specific proteins. Both metals concentrate to a lesser extent in the liver, and Cd accumulates also in the prostate, seminal vesicles, and vas deferens, thereby resembling Zn. A small fraction of these metals is excreted initially in the urine. The major fraction of the radioactivity administered is retained for long periods, and excreted slowly in the feces. The only radionuclides of this group which have been used for diagnostic studies are ^{197}Hg and ^{203}Hg.

Group III

The trivalent cations of the periodic Group III follow a fairly consistent pattern of behavior biologically, and concentrate predominantly in the skeleton. This includes the aluminum family of Group IIIB (B, Al, Ga, In, and Tl), Group IIIA transition metals (Sc, Y, and La), lanthanides, and actinides. In the aluminum family, B and Al have no radionuclides suitable for biological studies. Thallium is atypical because its stable state in neutral aqueous solutions is Tl^+ ion; hence biologically it resembles the alkaline metal univalent cations. It is readily absorbed from the gastrointestinal tract and has a uniform distribution in soft tissues, with a relatively high concentration in muscle and a lower concentration in bone compared with other members of Group III. Autoradiographically, some concentration of Tl has been noted in the thyroid of rabbits.

Other members of Group III are not absorbed from the gastrointestinal tract, tend to form complexes with serum and liver proteins, and are excreted in both urine and feces. The fraction excreted by way of the feces probably originates from the radioactivity concentrated in the liver and excreted in the bile. For Ga and In, 15 to 30% of the administered dose localizes in the skeleton and from 7 to 14% in the liver. The hepatic radioactivity has a biological half-life of 10 to 20 days and that of the skeleton approximately 2.5 years in the rat. The tissue localization of many elements of Group III varies remarkably between the carrier-free state and varying amounts of carrier element. For example, carrier-free Ga shows little tendency to concentrate in the skeleton, whereas carrier doses up to 5 and 10 mg per kilogram body weight show significant concentration in the skeleton up to 30% of the administered dose. Several members of the group are insoluble at the pH of plasma. Indium and Y, for example, concentrate in the skeleton when carrier-free, but with minute amounts of carrier they form insoluble colloids which localize in the reticuloendothelial system rather than bone. Gallium and Y exhibit a higher skeletal concentration than In, Sc, or La. The distribution of Group III elements in the skeleton differs from that of the alkaline earths, as demonstrated in autoradiographs. However, they probably do not deposit in osteoid tissue as was formerly thought. They appear to concentrate in the mineral fraction of bone on the available resorbing and highly mineralized non-growing surfaces by diffusion. Besides their skeletal localization, the lighter members of Group III (Ga, In, and Sc) exhibit some concentration in the musculature, up to 10 to 15% of the administered dose.

The more basic lighter lanthanons (Ce to Gd) with larger ionic radii tend to deposit in both the liver (25 to 50%) and skeleton (25 to 40%) and are excreted predominantly in the feces. In contrast, the more acidic and heavier lanthanons (Tb to Lu) with smaller atomic radii are deposited primarily in bone (50 to 60%) and only slightly in the liver (1 to 7%). They are excreted predominantly in the urine. The actinides exhibit similar behavior. Uranium is an atypical member of this group. Uranyl ions (UO_2^{++}), being divalent, tend to resemble Cd^{++} and Hg^{++} ions and concentrate in the renal cortex. The only member of Group III which has been used in medicine thus far is ^{68}Ga; however, ^{113}In and certain short-lived rare earth radionuclides show some promise as radioactive colloids or bone localizers.

Group IV

Periodic Group IVB includes the nonmetals C, Si, and Ge and the metals Ti, Zr, and Hf. The biological fate of C depends entirely upon the organic compound into which it is incorporated. The distribution of Si and Ti has not been studied. Under physiological conditions Ge exists as a hydrated anion; it tends to become distributed uniformly and excreted rapidly through the kidneys, like most anions. Other members of Groups IVA and IVB localize in bone mineral. For Sn and Pb, there is rapid elimination of 60% of the administered radioactivity in the urine and less than 10% for Zr. Fifteen to thirty per cent of the dose localizes in the skeleton, with prolonged retention. Hf is insoluble in neutral solutions, and in colloidal form localizes in the liver, with a lower concentration in the skeleton. None of the members of Group IV have been used for medical scanning applications.

Group V

Group VB consists of the nonmetals, N, P, and As and the metals Sb and Bi, with an oxidation state normally of +5. Following injection, phosphate has an initial high concentration in the liver and skeleton, but eventually about 90% of the residual activity is contained in the skeleton. Like C, the localization of N depends on the chemical nature of the compound. For As, both localization and toxicity vary greatly, depending on the valence state. The most common and stable pentavalent form (arsenate) becomes concentrated in the liver and is not retained in tissues but rapidly excreted in the urine. It is relatively nontoxic and does not inhibit most enzymes. On the other hand, the trivalent form (arsenite) is highly toxic and combines with the sulfhydryl groups of enzymes. It is excreted chiefly in the bile and feces, and approximately 50% is retained in the body for long periods. In rats, arsenate becomes tightly bound to circulating erythrocytes and therefore remains largely in the bloodstream. This binding is not observed in man. Antimonate, like arsenate, is rapidly eliminated by the kidneys. Bismuth differs from other members of the group. It usually exists as a trivalent oxygenated form in the bloodstream, bound to plasma proteins. It resembles the volatile divalent metals Cd and Hg and uranyl ions in concentrating to a high degree in the renal cortex. However, its retention time in the kidneys is shorter than that of the divalent metals, and it concentrates to a lesser extent in the liver, spleen, lung, and skeleton. Arsenic-74, a positron emitter, and ^{206}Bi have been used for brain tumor localization in man.

In Group VA, V and Nb become bound to plasma proteins and persist in the bloodstream. At 4 days, from 40 to 60% of the administered radioactivity is excreted in the urine and feces, and 10 to 15% is retained in the skeleton for long periods. Tantalum, being relatively inert and insoluble, becomes colloidal after injection and concentrates in the liver as well as the skeleton, with prolonged retention.

Group VI

Group VIB includes the elements O, S, Sc, Te,and Po. Sulfur-35 in the form of sulfate becomes rapidly and uniformly distributed throughout the intravascular and extravascular tissue fluid, and has been used in man for measurement of the total extracellular fluid volume. A small fraction specifically concentrates in the mucopolysaccharides of connective tissue and cartilage and attains its highest concentration in the marrow. The turnover of sulfate is apparently rapid in most tissues. The distribution of selenate and tellurate is similar but not identical to sulfate in experimental animals. In man, however, the plasma clearance of ^{75}Se selenate is more rapid than that of sulfate, and after 1 hour, incorporation into plasma proteins is demonstrated. In dogs, selenate has a biological half-life of about 7 days. Selenium-75 selenite is more reactive in vivo than selenate, exhibiting a faster plasma clearance, a higher concentration in the kidneys and liver, and a longer biological half-life (65 days) after the first 3 days. For both selenate and selenite, about 25% is excreted in the urine in the first 3 or 4 days. Polonium tends to form colloids, but nevertheless can be absorbed through the gastrointestinal tract; its highest concentrations are in the kidneys and spleen.

Group VIA includes the transition metals Cr, Mo, and W. The distribution of chromium depends on the valence state. In the hexavalent form (chromate) it becomes firmly bound to red blood cells, to a high degree in vitro and to a lesser degree in vivo. Such a small fraction of the chromate becomes eluted from red cells that this phenomenon is a widely employed labeling method for red blood cells. Most of the radioactivity persists within the cells until they are destroyed, chiefly in the spleen. The fraction of chromate remaining unbound to red cells and the chromate released by the destruction of red cells is promptly converted to the trivalent chromic form. Chromic ions readily form complexes and tend to become colloidal except in strongly acidic media. They become bound to plasma proteins, but 60 to 90% of the injected radioactivity is rapidly cleared from the plasma and excreted in the urine. The highest initial concentrations are in the vascular organs (kidneys, lungs, heart, liver, pancreas, and spleen), but these decrease rapidly. A small fraction is retained in the bone marrow and other reticuloendothelial cells for long periods. Although the initial accumulation in the testis is low, there is progressive accumulation for several days. There is some accumulation in the growing skeleton, but very little in the adult skeleton. When administered orally, in the trivalent state, less than 1% is absorbed from the gastrointestinal tract. There is slight absorption of molybdate and tungstate from the gastrointestinal tract. After injection, they are rapidly excreted by the kidneys. They concentrate slightly in bone without prolonged retention, following the typical pattern for anions. Red blood cells labeled with hexavalent ^{51}Cr and proteins labeled with trivalent ^{51}Cr have been employed in imaging applications in man.

Group VII

The halogens, or Group VIIB (F, Cl, Br, I, and At), have important differences in biological behavior and tissue localization. As a rule, they are readily absorbed from the gastrointestinal tract and are usually not retained for prolonged periods in soft tissues, but are promptly excreted by the kidneys with little or no fecal excretion. Fluorine has unique and rapid localization in the skeleton, up to 50 to 60% of the administered radioactivity. There is a highly selective trapping of iodide in the thyroid gland to a level of 15 to 40% of administered radioactivity at 24 hours. The fraction of iodide trapped in the thyroid gland becomes incorporated into the thyroid hormones and has a relatively long biological half-life of 60 to 138 days. Astatine also concentrates to some degree, and Br to a minimal degree in the thyroid gland. The halogens are secreted by the gastric mucosa, and this tendency increases with the atomic number in this series of elements. They are readily and completely reabsorbed in the small bowel. They accumulate and are excreted by the salivary glands and mucosal glands of the cervix.

The Group VIIA elements (Mn, Tc, and Re) are transitional metals. Manganese is an essential element of the body and is totally unlike the other two members of the group. When injected in the +2 oxidation state, it rapidly accumulates in the liver (25% of administered radioactivity), is excreted through the biliary tract into the gastrointestinal tract, and is not reabsorbed, but rather excreted in the feces. In addition, it accumulates in the pancreas and kidney--that is, in the organs rich in mitochondria. Lesser amounts also accumulate in the spleen, skeleton, thyroid, skin, small bowel, and muscle. Technetium and Re are most stable in heptavalent anionic form (TcO_4^- or ReO_4^-). They, like several other complex anions such as thiocyanate or perchlorate, behave as "pseudo-halogens" and mimic the localization of iodide. They are readily absorbed from the gastrointestinal tract and are concentrated transiently, but not organified, in the thyroid gland. They are secreted also by the salivary and gastric glands and readily eliminated by the kidneys. Unlike iodide and other halogens, however, they are only partially absorbed from the gastrointestinal tract, and up to 50% of an administered dose may be excreted in the feces. The short-lived radionuclide ^{99m}Tc has been of great interest in recent years as an agent for imaging applications.

Group VIII

The platinum metals include Fe, Co, Ni, Ru, Rh, Pd, Ir, Os, and Pt. Because of its unique role in red cell metabolism, Fe exhibits a complete individuality in biological behavior. It has a specific mechanism of selective absorption from the gastrointestinal tract, and is transported in the bloodstream in the beta-1 fraction of plasma globulin (transferrin). It is cleared rapidly from the bloodstream and localizes chiefly in the bone marrow and to a lesser extent in the spleen and liver. After several days, it re-enters the circulation incorporated in the circulating red blood cells. On destruction of the red cells in the spleen, it returns to the bone marrow, to enter the red cell metabolic cycle again.

Negligible quantities of Fe are normally excreted. The biological half-life is approximately 8 years in men and 3 to 4 years in menstruating women.

Cobalt, in ionic form, has a different localization and retention than Co incorporated in vitamin B_{12} (cyanocobalamin). Vitamin B_{12} is readily absorbed from the gastrointestinal tract, is bound to plasma proteins, and over several days is gradually cleared from the plasma and stored almost entirely in the liver. Urinary excretion does not occur unless the plasma proteins are saturated with vitamin B_{12}. The biological half-life of Co as vitamin B_{12} in the liver is as long as 400 days in man. On the other hand, cobaltous ion is only partially absorbed from the gastrointestinal tract and tends to concentrate in the glandular organs (liver, spleen, kidneys, and pancreas). Approximately 90% is readily excreted in the urine and 10% in the feces, as a result of biliary excretion.

The platinum metals other than Fe and Co, incorporated into vitamin B_{12} behave rather uniformly. The oxidation state of this group may vary widely from +2 to +8, with possibly different tissue localizations for different valences. They exhibit no tendency to colloid formation and are absorbed to some degree by the gastrointestinal tract. The major fraction is eliminated in the urine without prolonged retention. The heavier metals of this series tend to be eliminated even more rapidly than the lighter ones. Ruthenium is the only member that exhibits any retention whatsoever in the skeleton.

Despite the fact that the platinum metals have many gamma-emitting radionuclides with suitable energies and several desirable biological characteristics, they have not been used for imaging applications to any extent as yet. They may prove useful, however, in the future. The nuclide ^{52}Fe, a positron emitter with a half-life of only 8.2 hours, is quite suitable for medical application, particularly for bone marrow localization. Unfortunately, it can be produced only in a cyclotron and its preparation is time-consuming.

Group 0

The noble gases (Ne, Ar, Kr, Xe, and Rn) are chemically inert and have a limited solubility in aqueous media. Following inhalation or injection in aqueous media, they are rapidly eliminated by the lungs into the expired air with a biological half-time of only 5 to 10 minutes. They exhibit a preferential solubility in body fats, attaining a concentration of 10 to 20 times that of other tissues. Xenon-133m, ^{133}Xe, and ^{85}Kr are suitable gamma emitters for medical applications.

III. METHODS OF PRODUCTION OF RADIONUCLIDES USED AS TRACERS

A. Nuclear Reactors

1. Fission products

The fission process (Chapter IV) results in the formation of many radionuclides, both directly and from the decay of parent nuclides to radioactive daughter products. These are called fission products, and some have found application in nuclear medicine. The useful fission products must be separated chemically from the other radionuclides in spent reactor fuel elements. Examples of fission products that are used as tracers in medicine are ^{131}I, ^{132}I, ^{133}Xe, ^{85m}Kr, and ^{87}Kr. All fission products decay by beta emission.

2. Neutron activation

The principle of neutron activation is discussed in Chapter IV. A stable nuclide is activated to a radioactive isotope of the same element by means of the (n,γ) reaction initiated with thermal neutrons from a nuclear reactor. Many of the radionuclides used in nuclear medicine can be produced directly by neutron activation, namely, ^{59}Fe, ^{198}Au, ^{203}Hg, ^{137}Cs, ^{128}I, ^{99}Mo. Some others are daughter products of radionuclides which are produced in this manner, e.g., ^{99m}Tc is the daughter of ^{99}Mo which is produced by neutron activation. These parent-daughter relationships have led to the production of radionuclide "generators" which are discussed later in this chapter.

In order to produce radionuclides by neutron activation, a suitable target must be prepared and placed in the neutron beam. The irradiated target is processed either by dissolution or by more complicated separations such as ion exchange, precipitation and distillation to remove impurities or to concentrate the product nuclide. Radionuclides produced by neutron activation are generally beta emitters.

B. Cyclotrons

The cyclotron is a device that accelerates positively charged particles to very high energies by means of an alternating voltage applied across a gap between two large electromagnets. The particles are made to move in a circular path by applying a magnetic field perpendicular to their direction of motion. The high energy particles (protons or alpha particles) are made to strike a target material, thereby causing various types of nuclear reactions to occur. Many of the product nuclei are radioactive and have found application in nuclear medicine. Since radionuclides produced by cyclotrons generally have an excess of positive charge in their nuclei, they are likely to decay by either positron emission or electron capture. Decay by electron capture results in low energy x-ray emission plus, in some cases, an accompanying gamma photon. Hence, many cyclotron produced materials exhibit desirable properties for *in vivo* applications, i.e., x- or gamma-ray emission with no particulate radiation, thus enabling higher amounts to be administered with less patient dose.

Some radionuclides used in nuclear medicine that can be produced in cyclotrons are ^{125}I, ^{123}I, ^{68}Ga, ^{18}F. It is noteworthy that some radionuclides can be produced by more than one of the methods described.

C. Radionuclide Generators

The need for high photon fluxes without excessive radiation dosage to the patient makes short half-life radionuclides particularly attractive for in vivo studies. However, to use these effectively, one must be near a source of production of the nuclide. This has led to the production of so-called radionuclide generators. A generator consists of a column on which is adsorbed a long-lived parent material which decays to a shorter-lived daughter product. The parent material is produced in either a nuclear reactor or a cyclotron. The daughter product activity "grows-in" at a rate dependent on its half-life until it reaches equilibrium with the parent activity. (See Chapter III.) The daughter nuclide is then separated by chemical means and the parent is left to generate new daughter activity. The amount of daughter activity that can be separated at any time after a previous separation can be predicted from the series decay relationships given in Chapter III.

Generators have been developed for producing ^{132}I, ^{99m}Tc, ^{68}Ga, ^{87m}Sr and other nuclides in the laboratory. Typically these consist of a glass column containing aluminum oxide on which the parent material is firmly adsorbed. The alumina is retained in the tube by a porous glass disk. The daughter activity is eluted from the generator by pouring saline or some other reagent through the column and collecting the eluate in a suitable container. The entire generator may be shielded.

To date, eight generator systems have been developed to the point of commercial availability and many others look promising for the future.

SUGGESTIONS FOR FURTHER READING

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2. Blahd, W. H., Nuclear Medicine, McGraw-Hill Book Co. (1965), chap. 7.

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CHAPTER XVII

CLINICAL DIAGNOSTIC STUDIES PERFORMED AT THE RADIOISOTOPE LABORATORY, CINCINNATI GENERAL HOSPITAL

RADIOACTIVE IODINE THYROID UPTAKE STUDY

I. INTRODUCTION

The thyroid uptake helps to determine the thyroid gland's ability to take up inorganic iodine and retain it.

II. ISOTOPES UTILIZED AND APPROACH TO TECHNIQUE

Iodine-131 (sodium iodide) and iodine-123 (sodium iodide) are the two radionuclides used in this institution for thyroid uptake. Both isotopes are administered as an oral, tasteless liquid and metabolically duplicate the pattern of normally occurring stable iodine (iodine-127). If an uptake is requested as a single procedure, an activity of 10 microcuries (iodine-131) is used for adults. In small children and infants, 0.1 microcuries is utilized and the procedure is performed in the whole body counter. Other diagnostic procedures such as thyroid scanning, protein-bound iodine conversion ratio, and localization of thyroid metastases may require activities of from 50 microcuries to several millicuries. Iodine-123 (sodium iodide) in activities of 10 to 500 microcuries is a very suitable agent for diagnostic thyroid studies, for with equivalent activities, the radiation dose to the thyroid gland from iodine-123 (sodium iodide) is less than that for iodine-131 (sodium iodide) by a factor of approximately 30. Twenty-four hours after the administration of the agent (iodine-131 or iodine-123), the patient returns to the laboratory and measurements of the activity of the thyroid gland and the thigh are obtained. The thigh counting is performed so that an indication of the activity present in tissue behind the thyroid gland may be obtained. In patients who have a low uptake of radioiodine (less than 15%) due to chemical block, myxedema, or cardiac failure, the extrathyroidal radioactive iodine is usually increased. This thigh count activity is subtracted from the thyroid gland activity to obtain the activity within the thyroid gland. A standard (an aliquot of the radioactive iodine given the patient) is procured and counted in exactly the same manner as the thyroid gland of the patient. By comparing the counting rate from the standard to the net counting rate from the patient's thyroid gland, the percentage uptake of the radioactive iodine by the thyroid is determined by the following formula:

$$\text{thyroid uptake (\%)} = \frac{\text{net cpm thyroid - net cpm thigh}}{\text{net cpm standard}} \times 100$$

Since the absolute quantity of iodide in the extra-thryoidal pool is usually not known, one cannot determine the absolute value of iodide accumulation in mass per unit time. The result measures the fraction of the extra-thyroidal iodide pool that is being accumulated per unit time.

This procedure is valid since an overactive thyroid gland turns over the plasma iodide pool faster than a normally active gland, and an underactive gland turns over iodide more slowly, provided the body's iodide stores are in the usual range.

Circulating iodide is ultimately disposed of by two competing mechanisms, i.e., thyroid uptake and urinary excretion. Urinary excretion, in general, bears a reciprocal relationship to thyroid function. Urinary excretion of less than 40 percent of the tracer dose in 24 hours (24 hour collection) are consistent with the diagnosis of hyperthyroidism. Excretions in excess of 40 percent are usually associated with normal or decreased thyroid function.

III. RATIONALE

The normal range for this procedure is 15-45%, thereby yielding a direct appraisal of thyroid function, e.g., hypothyroidism, euthyroidism, or hyperthyroidism. Any iodine-containing preparations, either for external or internal use are contraindicated prior to this procedure, as the thyroid gland becomes saturated with iodine and this iodine chemically "blocks" the uptake of the radioactive iodine.

PROTEIN-BOUND IODINE CONVERSION RATIO TEST

I. INTRODUCTION

The Protein-Bound Iodine Conversion Ratio measures the thyroid gland's ability to convert radioactive inorganic iodine to protein bound radioactive iodine in the plasma, i.e., the inorganic iodine in the thyroid is principally converted to radiothyroxine and tri-iodothyronine, part of which is secreted into the bloodstream where it forms a protein complex. The amont of administered radioactive iodine which is converted within a given period of time is a measure of thyroid function.

II. ISOTOPES UTILIZED AND APPROACH TO TECHNIQUE

Iodine-131 (sodium iodide) is the agent of choice. If an RAI Uptake and PBI Conversion Ratio are requested, the usual adult activity administered is 50 microcuries of Iodine-131 (sodium iodide) whereas if a thyroid scan is also requested, the procedure may be performed with 100 microcuries of sodium iodide. The patient is given the activity of radioiodine and returns 24 hours later for the PBI Conversion Ratio. A heparinized venous blood sample is centrifuged and activity present in the plasma sample is determined in a suitable scintillation well counter. The activity in this sample represents both the inorganic radioiodine and the protein-bound radioiodine. The plasma is then transported through an ion exchange resin column by gravity, which removes the inorganic radioiodine, permitting the protein-bound iodine to remain in the plasma. This sample is counted with the same instrumentation and the counts are converted into a percentage of protein-bound radioactive iodine.

III. RATIONALE

The normal values for this procedure closely approximate those for the RAI Uptake. Some thyrotoxic glands are so active that the 24 hour RAI Uptake has fallen to within the normal range, but since a large amount of thyroxine has been released, the conversion ratio is elevated. This test is often invalidated by congestive heart failure or renal dysfunction.

TSH STUDY

I. INTRODUCTION

This study is a test for assisting in the diagnosis of certain thyroid states by noting the effect upon the radioactive iodine uptake after the patient has received thyroid stimulating hormone.

II. ISOTOPES UTILIZED AND APPROACH TO TECHNIQUE

Iodine-131 (sodium iodide) and iodine-123 (sodium iodide) may be used. An initial 24-hour RAI Uptake should be performed. Subsequently, the patient is given 10 units (2.5 mg) of thyroid stimulating hormone intramuscularly each day for three days. Injections of TSH are contraindicated in those patients in whom angina pectoris is present, and certain allergic manifestations have been noted on occasion. It has been our practice to have the patient remain in the department for a least 30 minutes after the injection of TSH to note any adverse effects. On the third day, with suitable instrumentation, a baseline RAI Uptake is performed prior to the second tracer dose (this is a check for the residual radioiodine from the initial RAI Uptake). Suitable activity of radioiodine is then administered to the patient and a second RAI Uptake is obtained 24 hours later. The difference between the two uptakes indicates the response of the thyroid gland to TSH.

III. RATIONALE

Primary hypothyroidism may be distinguished from secondary hypothyroidism by the use of the TSH procedure. Primary hypothyroidism shows no significant elevation in uptake after TSH (example: initial RAI Uptake = 5%, TSH Uptake = 6%). By contrast, secondary hypothyroidism shows a marked increase in uptake (example: initial RAI Uptake = 5%, TSH Uptake = 40%), and is considered to be due to anterior pituitary dysfunction. It is a test that cannot be performed as quickly as the 24-hour RAI Uptake alone, but one which may provide more definitive information as to the presence of potentially functioning thyroid tissue which has been suppressed or lacks stimulation from the pituitary.

T-3 SUPPRESSION STUDY

I. INTRODUCTION

The T-3 Suppression Study (tri-iodothyronine test) is a method used to assist in determining the presence or absence of an autonomous thyroid gland or nodule which is not under normal control by the pituitary, and in finding hyperthyroidism without hypermetabolism.

II. ISOTOPES UTILIZED AND APPROACH TO TECHNIQUE

Iodine-131 (sodium iodide) and iodine-123 (sodium iodide) are utilized for this procedure. An initial RAI Uptake is performed on the patient. Subsequently, the patient is given 75 micrograms of cytomel (T-3) per day, orally, in three divided doses for seven days. Cytomel is contraindicated in those patients with severe cardiac disease. On the seventh day, a baseline RAI Uptake is performed to check for residual radioactive iodine in the thyroid gland and then adequate activity of radioactive iodine is administered orally. A second RAI Uptake is performed 24 hours later, subtracting the baseline activity present to obtain an accurate thyroid uptake.

III. RATIONALE

This procedure is particularly beneficial in those cases that have borderline high RAI Uptakes initially. These patients with normal thyroid function reveal a significant depression with the T-3 Suppression Uptake --usually a reduction of from 60-80% from the initial RAI Uptake. If there is a significant depression of the RAI Uptake, the patient is considered to be euthyroid. Situations which reveal no significant depression of uptake are Grave's disease, hyperthyroidism in remission, or autonomous adenomas ("hot" nodules) with normal thyroid uptake values. Since the T-3 Suppression Study does not alter the radioactive iodine uptake of the thyroid gland in the hyperthyroid patient, the test affords a method of differential diagnosis and still enables the physician to treat the condition with radioactive iodine therapeutically, if desired.

T-3 RESIN UPTAKE STUDY

I. INTRODUCTION

The T-3 Resin Uptake is an *in vitro* method of determining indirectly the amount of circulating thyroid hormone by measuring the amount of TBG (thyroid-binding globulin) in the patient's serum that has been bound by tri-iodothyronine, and thereby utilizing this information as an estimation of thyroid function.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Iodine-131 (sodium iodide) labeled T-3 (tri-iodothyronine) is used in this resin ion exchange procedure and may be obtained in kit form from radiopharmaceutical manufacturers. One of three milliliters of the patient's serum is required for this test, so it affords a quick method of assaying thyroid function without giving the patient any radioactive materials. In the appropriate container, a resin sponge is added to a mixture of 2 ml serum and iodine-131 labeled T-3. With a suitable scintillation well counter, the activity present is calculated. After an incubation period of one hour, the fluid contents of the container are aspirated. Several washings of the sponge are performed, aspirating the fluid content with each washing. Again the activity is calculated from the resin sponge. By calculating the percentage uptake remaining in the resin sponge after washings, as compared to the initial mixture of serum labeled iodine-131 and sponge, an indirect method for obtaining the binding index of tri-iodothyronine in the patient's serum is obtained.

III. RATIONALE

The normal adult range is 25-35%, greater than 35% indicating the hyperthyroid range and less than 25% the hypothyroid range. There are many medications and clinical conditions, such as pregnancy, that will affect the results of this test. The radiopharmaceutical manufacturers supply an excellent list of these medications and conditions, and the effect they have upon this procedure. Used properly, this test is intended as an easy method of screening thyroid disease. It is particularly useful as a laboratory aid and in the diagnosis of hyperthyroidism associated with pregnancy.

THYROID CANCER WORK-UP

I. INTRODUCTION

One of the most elaborate diagnostic procedures in nuclear medicine is the thyroid cancer work-up. This work-up may be utilized before or after surgery and as a method of evaluating the extent of certain cancers.

II. ISOTOPES UTILIZED AND APPROACH TO TECHNIQUE

Usually, iodine-131 (sodium iodide) is utilized. If a patient has suspected cancer of the thyroid, yet surgery has not been performed, the usual activity (100 microcuries) for an RAI Uptake and thyroid Scan is employed. If thyroid cancer is suspected clinically and per scan, biopsy and/or surgery is usually performed. If cancer is proven, radical thyroidectomy is sometimes performed, possibly removing most of the thyroid gland. Postoperatively, the patient is given a larger activity of the radioactive iodine (usually 1 to 2 millicuries) with or without TSH (Thyroid Stimulating Hormone) injections in order to reveal remnants of thyroid tissue after surgery and metastatic areas throughout the body.

Physiologically, once the thyroid gland has been ablated, metastatic tissue elsewhere in the body often concentrates the radioactive material, thus making it possible to reveal metastatic areas in the neck, chest, bone, soft tissue, or lymph glands.

III. RATIONALE

If only a portion of the thyroid gland is excised, large activities of radioiodine (e.g., 100 millicuries) are sometimes used to ablate the remaining thyroid tissue. Serial thyroid cancer work-up checks every 6-12 months are then instituted.

TRIOLEIN FAT ABSORPTION STUDY

I. INTRODUCTION

The Triolein Test is dependent on the absorption of hydrolyzed tagged triolein from the gastrointestinal tract.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Iodine-131 (sodium iodide) has been found suitable as a label for fat and fatty acids. The neutral fat utilized for labeling purposes is glyceryl trioleate (triolein). In the body, the iodine-131 (sodium iodide) triolein behaves like a neutral fat; i.e., it is hydrolyzed by pancreatic lipase to glycerol and oleic acid before absorption in the intestinal tract may take place. In the blood, the iodine-131 triolein exists in two forms--lipid-bound iodine-131 triolein and inorganic iodine-131 resulting from a metabolic breakdown of the labeled fat. On the day prior to the study, ten drops of a saturated solution of KI is administered orally three times (after each meal) to block iodine-131 uptake by the thyroid gland. The patient should fast from midnight the day prior to testing and should not have received any medications affecting pancreatic function for at least 48 hours prior to testing. The iodine-131 triolein is administered orally in capsule form. The patient is not permitted to eat or drink during the procedure. Heparinized blood samples are obtained 2, 3, 4, 5, and 6 hours after administration of the iodine-131 triolein. The height and weight of the patient are obtained and the estimated whole blood volume of the patient is determined by Retzloff's formulae.

Estimation of Erythrocyte and Plasma Volume
According to Height and Body Weight

Formulae for Men:

Erythrocyte volume (ml) =
$8.2 \times \text{height (cms)} + 17.3 \times \text{weight (kgm)} - 693 \pm 252$ ml (1 S.D.)

Plasma volume (ml) =
$23.7 \times \text{height (cms)} + 9 \times \text{weight (kgm)} - 1709 \pm 358$ ml (1 S.D.)

Formulae for Women:

Erythrocyte volume (ml) =
16.4 × height (cms) + 5.7 × weight (kgm) - 1649 ± 129 ml (1 S.D.)

Plasma volume (ml) =
40.5 × height (cms) + 8.4 × weight (kgm) - 4811 ± 196 ml (1 S.D.)

An aliquot of each blood sample is counted in a suitable well-type scintillation counter and the per cent of blood absorption of iodine-131 triolein is obtained.

III. RATIONALE

This test is performed to screen for impaired fat digestion and/or decreased intestinal absorption. Thus, should this test be within normal range, good pancreatic function and the existance of normal fat digestion and absorption is inferred. An iodine-131 Oleic Acid Fat Absorption Study is indicated should the iodine-131 Triolein Fat Absorption Test be abnormal.

OLEIC ACID FAT ABSORPTION STUDY

I. INTRODUCTION

In the absence of pancreatic lipase (a pancreatic enzyme), iodine-131 triolein cannot be absorbed. If the Triolein Fat Absorption Test has been performed and found to be abnormally low, an iodine-131 Oleic Acid Study is indicated, since oleic acid does not require hydrolytic action of pancreatic lipase to be absorbed, and thus measures the efficiency of small bowel absorption.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Iodine-131 has been found suitable as a label for this fatty acid. The patient preparation and procedure are exactly the same as for the iodine-131 Triolein Fat Absorption Study except that iodine-131 oleic acid is utilized.

III. RATIONALE

A high blood level with iodine-131 oleic acid following a low blood level with iodine-131 triolein is indicative of pancreatic lipase deficiency. A low blood level of both iodine-131 triolein and iodine-131 oleic acid suggests that neither neutral fats nor fatty acids are absorbed. This may be due to absorptive defects in the small bowel, a rapid transit time, or decreased absorptive area. These tests give 80% confidence of the diagnosis of normal or malabsorption.

IRON KINETIC STUDIES

I. INTRODUCTION

Iron kinetic studies measure the rate of disappearance of iron from the plasma, the plasma iron turnover rate, and the utilization of iron in red blood cell production. The clearance of iron from the plasma is of value in determining total bone marrow activity, i.e., the total amount of iron being incorporated into hemoglobin in the bone marrow, but since the amount of nonradioactive iron in the serum will influence this rate, a determination of the plasma iron turnover rate represents an attempt to refine the clearance study. The red cell utilization technique requires that the iron not only leave the plasma, but that it also be moved into the red cells. Therefore, it is helpful in evaluating effective bone marrow function which is reflected in the percentage of labeled red blood cells in the peripheral circulation at 10 to 14 days.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Ferrous citrate-59 is employed for this test. The patient should be in a fasting state for the test and, prior to the injection of the isotope, a serum iron blood sample should be obtained. The ferrous citrate-59 is injected intravenously and serial blood samples are drawn 20, 30, 60, 90, 120, and 180 minutes post-injection and then at 24 hours, and at two to three day intervals for a period of approximately 28 days. At 4 hours, 24 hours, and at the two to three day intervals, external measurements of activity are made with appropriate instrumentation over the precordium, spleen, liver, and sacral areas.

III. RATIONALE

The iron red cell utilization is decreased in aplastic and other anemias where the bone marrow is ineffective in its red blood cell production. In normal patients, 70-95% of the ferrous citrate-59 is utilized in the red blood cells by the 14th day of testing. Also, the external measurements of ferrous citrate-59 made over the bone marrow blood pool, and the reticuloendothelial tissue (spleen and liver) may help in the evaluation of bone marrow function.

IRON BINDING CAPACITY TEST

I. INTRODUCTION

This test affords a quick, easy, and accurate method of measuring the unsaturated iron-binding capacity of the serum.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Ferrous citrate-59 is employed and the complete testing apparatus is commercially available in kit form. The test employs ferrous citrate-59 along with a polyester foam sponge in which is embedded a finely divided ion exchange resin. The test is performed in vitro with the patient in a fasting state. Venous blood is drawn, and plasma is obtained through centrifugation. By counting the activity present in the resin sponge before and after washings with tap water, the per cent resin sponge uptake is derived.

III. RATIONALE

Once the per cent resin sponge uptake is obtained, the results of the test are expressed as unsaturated (latent) iron-binding capacity. These results are obtained through a mathematical computation involving the activity (net counts per minute) of the sponge before and after washings, and the micrograms of iron added to the test kit syringe. The results are reported as micrograms Fe/100 ml of the patient's serum. This result is valuable in such clinical situations as iron deficiency anemia, anemia of chronic infection, and hemochromatosis.

HYPOPROTEINEMIA TEST

I. INTRODUCTION

Nuclear medicine has introduced an easy method of determining the presence of gastrointestinal protein loss. This condition is present in a variety of clinical situations, and may be caused by the loss of plasma protein into the intestinal lumen.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Although other agents have been utilized such as radioiodine B_1 human serum albumin and radioiodine-125 human serum albumin, the agent of choice is sodium chromate-51 labeled albumin. (The label must be made in the laboratory if not obtainable commercially.) Sodium chromate-51 may be firmly bound to albumin. Normally, only a small percentage of chromium-tagged albumin in the vascular system enters the gastrointestinal tract, so there is marked difference in fecal excretion of the isotope between normal patients and those with loss of protein plasma through the intestinal wall. The appropriate activity of the sodium chromate-51 labeled albumin is intravenously administered and subsequent stool collection is made for a period of four days. The activity in the stool is quantitated with proper instrumentation and the per cent excretion of the isotope is calculated.

III. RATIONALE

This test is used to rule out exudation of protein into the bowel lumen as a cause of hypoalbuminemia found in such diseases as exudative enteropathies, ulcerative colitis, sprue, regional enteritis, and gastric neoplasia. It affords the physician with information that may be utilized in treating the above conditions.

FIRST STAGE SCHILLING TEST

I. INTRODUCTION

The Schilling test is used to diagnose vitamin B_{12} malabsorption states, as occur in pernicious anemia, a form of megaloblastic anemia resulting from the lack of secretion of intrinsic factor, postgastrectomy anemias, and various diseases associated with malabsorption. Intrinsic factor is present in the normal secretions of the stomach and is necessary for the absorption of vitamin B_{12} by the ileum. The test is based upon the fact that when primary binding sites, the liver and plasma, are saturated by a large parenteral dose of B_{12}, any excess over that taken up by the liver is excreted in the urine.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Cobalt-57 (cyanocobalamin) labeled vitamin B_{12} is most frequently utilized. The patient should fast from midnight the day prior to testing and should not have had vitamin B_{12} in any form for at least 5 days. The cobalt-57 is administered orally in liquid form and 24 hour urine collection is initiated. Two hours after the cobalt-57 activity is administered, a "flushing dose" or "saturation dose" of vitamin B_{12} (1,000 micrograms) is administered intramuscularly to saturate all binding sites. Should the patient have renal dysfunction, it may be necessary to collect three days of urine with a "flushing dose" of vitamin B_{12} given each 24 hours.

III. RATIONALE

After the labeled vitamin B_{12} is given orally, the stable vitamin B_{12} is administered to increase excretion; the radioactivity appears in the urine. The activity present in the urine is proportional to the absorption of the labeled vitamin B_{12} and therefore an indirect measurement of the presence or absence of intrinsic factor or defective vitamin B_{12} absorption.

Abnormal values of the First Stage Schilling test suggest either pernicious anemia, or non-specific malabsorption of many possible etiologies assuming normal renal function. Normal values point to a deficiency of folic acid as the cause of megaloblastic anemia.

SECOND STAGE SCHILLING TEST

I. INTRODUCTION

The Second Stage Schilling test is performed on those patients who have abnormally low First Stage Schilling results. This procedure will help to confirm or deny the presence of pernicious anemia.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Again, cobalt-57 (cyanocobalamin) labeled vitamin B_{12} is the agent used. The patient preparation and test are exactly the same as for the First Stage Schilling except that an intrinsic factor concentrate capsule (60 mg) is administered at the same time as the cobalt-57 labeled vitamin B_{12}. A period of 5 to 7 days should elapse between the First and Second Stage Schilling procedures.

III. RATIONALE

Markedly improved excretion of the cobalt-57 labeled vitamin B_{12} after intrinsic factor confirms the diagnosis of intrinsic factor deficiency. Should the Second Stage Schilling result be low, "the blind loop syndrome" or other causes of malabsorption may be present and a Third Stage Schilling procedure should be performed.

THIRD STAGE SCHILLING TEST

I. INTRODUCTION

The Third Stage Schilling test is performed on those patients who have low excretion of cobalt-57 labeled vitamin B_{12} in the urine with the First and Second Stage Schilling tests.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Cobalt-57 (cyanocobalamin) labeled vitamin B_{12} is the agent used. Patient preparation and the test are exactly the same as the First Stage Schilling except that the patient should receive tetracycline, 250 milligrams, four times a day for 10 days prior to the test. Tetracycline is administered to reduce or alter intestinal bacteria in the possible blind loop syndrome.

III. RATIONALE

Markedly improved excretion of labeled vitamin B_{12} after tetracycline confirms the presence of malabsorption secondary to interference with the normal absorptive process by the bacterial flora which compete for the vitamin B_{12} within the body. This situation may occur with the blind loop syndrome, or after certain gastrectomy procedures.

BONE SCANNING

I. INTRODUCTION

The major application of bone scanning is the detection of bone abnormalities prior to radiographic evidence or the confirmation of those conditions which are noted on radiographs.

II. ISOTOPE UTILIZED

Strontium nitrate-85 injected intravenously is the agent most commonly utilized. It is handled by the body similarly to calcium, accumulating in areas of tumor-laden bone in greater concentration than in normal bone. Scanning may be started 48 hours post-injection, but it is generally conceded that the best time to obtain good localization in areas of abnormality is at 5 to 7 days post-injection. If the pelvic area is to be scanned, the patient should receive enemas at least 24 hours prior to scanning, as the strontium nitrate-85 is excreted into the bowel and may be present in the colon at the time of scanning. It is routine in this institution to perform scans on the entire spine and pelvic area both anteriorly and posteriorly. Other areas are scanned as indicated.

III. RATIONALE

Bone scanning yields positive scans in a number of situations such as fractures, metastatic bone disease, osteomyelitis, and neoplasma. It is impossible to differentiate these diseases by scan, but by comparing x-rays, scans and the clinical symptoms of the patient, one may obtain added information about the clinical state. An example would be a female with a previous radical mastectomy who has marked pain in the lumbar spine area. X-rays show no metastatic disease, but bone scans show a marked localization of the strontium nitrate-85 in certain areas of the lumbar spine. This information would aid the radiotherapist in diagnosing metastases and localizing areas to be treated. Since strontium nitrate-85 remains in bone for a long period of time, it is possible to scan as long as one month post-injection.

BRAIN SCANNING

I. INTRODUCTION

The brain scan is accepted as a routine clinical procedure both for screening and follow-up of certain brain diseases. It has proven to be most beneficial in the localization of brain tumors, vascular abnormalities including infarctions and hemorrhage, and abscesses. Radiopharmaceuticals utilized for brain scanning are characterized by the fact that normal brain tissue is relatively or completely impermeable to their passage from the blood. Brain tumors and most other mass lesions, however, are much more permeable than normal brain tissue, the degree and permeability varying with the type of lesion and agent for scanning.

II. ISOTOPES UTILIZED

Although several radionuclides are utilized for this procedure, the most common is ^{99m}Tc (pertechnetate). Technetium-99m (pertechnetate) is obtained from a Molybdenum-99 generator, which consists of a shielded aluminum oxide column from which the pertechnetate can be eluted daily. A relatively large amount of this material may be injected intravenously because the short physical half-life of 6 hours and the lack of beta particle radiation gives a small absorbed dose to the patient. The high gamma activity results in a greatly increased counting rate compared to other agents and, as a result, faster scanning speeds (four views with rectilinear scanning requires approximately 40 minutes) with greatly improved counting statistics. Utilizing this radionuclide for brain scanning, it is necessary for the patient to receive 200 mg of potassium perchlorate in two ounces of flavored vehicle orally approximately two hours prior to scanning. This medication partially blocks the uptake of ^{99m}Tc (pertechnetate) in the thyroid gland, choroid plexus and salivary glands, thus removing confusing areas of isotope localization.

Other scanning agents that may be utilized are ^{197}Hg chlormerodrin (neohydrin), ^{203}Hg chlormerodrin (neohydrin), and iodine-131 serum albumin (radioiodinated human serum albumin). These radiopharmaceuticals are injected intravenously and after an appropriate waiting period (1 to 24 hours) scanning may begin. To perform the routine views of the brain (anterior, posterior, left and right laterals), the 3 inch rectilinear scanning time is approximately 30-40 minutes per view, thus requiring a minimum of 2 to 3 hours per brain scan for the latter three isotopes.

III. RATIONALE

The brain scan is an adjunctive diagnostic aid in detecting and localizing intracranial primary and metastatic neoplasms, abscesses and vascular abnormalities such as subdural hematoma, A-V malformation and cerebral infarct, and hemorrhage. Any patient may safely receive these radiopharmaceuticals, whereas arteriography and pneumoencephalography are sometimes contraindicated by the clinical status of the patient. It is generally conceded that brain tumors, abscesses and most vascular abnormalities result in increased permeability of the normal brain to the isotope. Since ^{99m}Tc (pertechnetate), when injected intravenously concentrates in these abnormal areas, the above conditions result in increased radioactivity, thereby giving a "hot spot" on the scan and/or direct information regarding the existence, size and location of the abnormality. This localization is particularly helpful to the neurosurgeon for it will aid him in deciding the location and size for a bone flap in his surgical approach. It also helps the radiologist in planning therapeutic irradiation.

MEDIASTINAL SCANNING

I. INTRODUCTION

One of the least frequently utilized procedures in nuclear medicine, yet one that may be of great value, is mediastinal scanning. It is a diagnostic procedure to help differentiate between vascular and solid mediastinal masses, cardiomegaly and pericardial effusion.

II. ISOTOPES UTILIZED

Many different radionuclides have been used for the pericardial scan. The most frequently used are ^{99m}Tc-albumin, ^{99m}Tc (pertechnetate) and radioiodine-131 human serum albumin. With radioiodine-131 human serum albumin there is a comparatively high radiation dose delivered to the patient, and also the scanning speed is very slow (requiring approximately 30-60 minutes). Critically ill patients cannot usually tolerate lying flat for this period of time. By contrast, large amounts of ^{99m}Tc (pertechnetate) may be injected because its short physical half-life and lack of beta particle radiation give a small absorbed dose to the patient. The high gamma yield allows a much faster scanning speed and required only 10-15 minutes for the entire procedure. Most critically ill patients can tolerate this procedure if ^{99m}Tc is utilized.

III. RATIONALE

Upon completion of the pericardial scan, a six or seven foot recumbent chest x-ray is obtained with the patient in exactly the same position as for the scan. Lead markers are placed at the supra-sternal notch and xiphoid. This film is taken to determine the magnification of the cardiac image on the film by a comparison of the distances between the lead markers on the photoscan and the roentgenogram. Normally, the photoscan outline of the heart (intracardiac blood pool) closely approximates the outline of the heart as seen on the chest x-ray. Pericardial effusion produces obvious departures from the normal pattern, i.e., the greatest transverse diameter of the heart on the chest x-ray is much wider than the blood pool on the photoscan. Since the ^{99m}Tc (pertechnetate) is excreted by gastric mucosa and pooled in the liver due to its great blood supply, these organs are readily discerned on the scan. If pericardial effusion is present, the intracardiac pool of radioactivity is widely separated from the gastric mucosa and the liver, thereby giving a "halo" effect around the heart due to the absence of radioactivity in pericardial fluid.

By comparing the scanning pattern with the chest roentgenogram, it is possible to differentiate mediastinal masses (e.g., neoplasms) from aneurysms.

RENAL SCANNING

I. INTRODUCTION

Renal scanning has long been a valuable diagnostic tool and particularly so if utilized in conjunction with the intravenous pyelogram. Problems which occur in kidney radiology such as overlying gaseous shadows, overlapping organs and confusion with other structures are avoided by renal scanning. It is sometimes useful when a patient is allergic to the contrast medium used for the pyelogram.

II. ISOTOPES UTILIZED

Hg-197 chlormerodrin (neohydrin) and ^{203}Hg chlormerodrin (neohydrin) are agents of choice. Passage of the radioactivity through the kidney is slow enough to outline the kidney for several hours. These agents are very sensitive in the detection of viable renal tissue, since chlormerodrin is concentrated in the renal tubular cells. The agent is injected intravenously and scanning may begin in one hour with an approximate scanning time of 30 minutes. Scanning should be performed with the patient in the prone position. With depressed renal function, increased hepatic uptake is noted on the scan.

When a physician is attempting to differentiate between a cyst or tumor of the kidney, the patient is injected with the ^{197}Hg chlormerodrin, scanned, and without moving is reinjected with ^{99m}Tc (pertechnetate) and a very rapid scan of the effected kidney is performed. The ^{197}Hg chlormerodrin scan would depict a void or "cold spot" in the affected area of the kidney if it is a cyst or solid tumor, whereas with the ^{99m}Tc renal scan, the affected area would fill if a tumor is present or remain void if a cyst is present. This affords a quick method of differential diagnosis.

III. RATIONALE

The main indication for the use of renal scanning is identifying mass lesions of the kidney such as tumors, cysts, abscesses, etc., and noting the size, shape and location of the kidneys. Satisfactory visualization is another indication of adequate renal function. The renal scan can also be used as a follow-up after renal transplants to determine if the transplant is viable, as well as determining agenesis of a kidney.

Since there are no contraindications for this procedure except pregnancy, it may be used in cases of allergy to iodine (the radiopaque contrast medium used for pyelograms contains iodine), acute or chronic renal dysfunction or renal diseases. The size, contour and position of each kidney may be determined along with some indication of kidney function.

LIVER SCANNING

I. INTRODUCTION

A very valuable diagnostic procedure in nuclear medicine is liver scanning. Since heretofore the only method of procurring an anatomic diagnosis has been by angiography and/or a laparotomy, this test affords a simple, accurate way of obtaining the anatomic information for the management of some liver diseases.

II. ISOTOPES UTILIZED

Three radionuclides are commonly utilized. Iodine-131 labeled rose bengal is administered intravenously and is taken up rapidly by the polygonal cells of the liver and excreted with bile through the biliary tract into the bowel. The concentration of this agent in the liver changes during the time the liver is being scanned. By positioning a scintillation probe over the liver area and another probe over the ear, and connecting the probes to strip-chart recorders, a test of liver function may be obtained, for the liver uptake of iodine-131 rose bengal and blood activity of the isotope in other areas of the body are inversely proportional. Since most blood chemistry measurements of liver dysfunction are dependent upon colorimetric procedures, and this test is dependent on concentration of radioactivity, valid results are extended to the entire spectrum of liver damage despite the depth of jaundice. A liver scan is performed after the liver function study is completed. Excretion into the intestine via the biliary tract may result in confusing abnormal activity. However this agent provides a means of demonstrating biliary obstruction. Scanning is begun at the lower liver margin and proceeds upward to avoid the heavy confusion by the material that enters the intestinal tract. The other two commonly utilized radionuclides for liver scanning are ^{99m}Tc sulfide colloid and ^{198}Au colloid. These colloid particles are phagocytized by the Kupffer cells of the reticuloendothelial system. These phagocytized particles remain in the Kupffer cells of the liver almost indefinitely. These materials have a particle size varying from 0.005 and 0.05 microns with an average size of 0.039 microns. Besides defining the anatomy and position of the liver, the scans obtained with these agents also yield the valuable information of size, shape, and position of the spleen which is immediately adjacent and to the left of the liver, which is sometimes confused clinically with the left lobe of a very large liver.

III. RATIONALE

One of the major applications of liver scanning is the differentiation of solitary or multiple local lesions or space occupying lesions from diffuse parenchymal disease of the liver such as cirrhosis or hepatitis. Therefore, when diffuse parenchymal disease of the liver is suspected clinically, an iodine-131 rose bengal scan can be obtained to determine the function, size, and shape of the liver. Earmarks of diffuse disease by scan using iodine-131 rose bengal are a rather "patchy" or "salt and pepper" type uptake of the material within the liver, increased concentration of the material in the area of the heart, increased background activity, and little or no activity in the bowel. If by contrast a lesion or void spot of radioactivity is noted within the liver, this may indicate a primary tumor, metastases, fatty infiltration, infarct, abscess or cyst is present. This information aids the surgeon as to the location of the exact area from which a biopsy may be obtained. Another liver scan may then be obtained with ^{198}Au colloid or ^{99m}Tc sulfide colloid to confirm the area under suspicion. It has been shown clinically that lesions 2.5 cm or larger can be detected on a liver scan.

LUNG SCANNING

I. INTRODUCTION

With the high incidence rate of pulmonary emboli and other lung diseases, a quick, accurate method of screening for suspected pathology becomes necessary. Incorporated with a six foot recumbent chest x-ray, the lung scan is a very valuable diagnostic tool.

II. ISOTOPE UTILIZED

Technetium-99m MAA (macroaggregated albumin) is the agent of choice, as scanning time is extremely short and it is not necessary to block the thyroid gland with SSKI (saturated solution potassium iodide). Iodine-131 MAA (radioiodinated human serum albumin macroaggregate) is the other agent utilized in lung scanning. The dose of MAA should not exceed 0.1 mg protein per kilogram body weight. The large aggregates of serum albumin are composed of innumerable minute particles in loosely knit masses ranging in size from 20-50 micros in diameter. These particles when injected intravenously mix uniformly in the blood. Hemodynamic and gravitational forces affect the particles in a similar manner to that of red blood cells. The particles wedge temporarily in the pulmonary capillaries, remaining there for a few hours until they are fragmented and reenter the circulation. During this time lapse, the lung scan is performed. It is desirable to administer SSKI in a dose of ten drops at least two hours prior to scanning time and ten drops three a day after the scan in order to minimize the uptake of radioactive iodine in the thyroid gland.

III. RATIONALE

Pulmonary scanning is used as an adjunct to other diagnostic procedures whenever information is desired about pulmonary vasculature. The most important use is to confirm or rule out pulmonary emboli. Even in critically ill patients, this scan is an easy, quick and safe way to determine the site and extent of emboli. It is most useful when a patient has acute chest pain, a chest x-ray is obtained and there is no evidence of infiltrate or atelectasis. Acute pulmonary emboli are usually demonstrable on lung scan before there is x-ray evidence of the same. Other useful information is provided by the scan in the diagnosis of various types of malignancies affecting the lungs, pneumonia, cysts or bullae, atelectasis, pleural effusion, abscesses, emphysema, and chronic asthma.

PANCREATIC SCANNING

I. INTRODUCTION

The pancreas is one of the most difficult organs in the body to scan. This is in part due to the anatomical location of the organ and also the problem of finding an isotopic compound that will selectively localize within the pancreas. Successful scanning of the pancreas represents an important contribution to diagnostic medicine, since there is no single and direct method for evaluating pancreatic function and morphology.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

The agent of choice to date for pancreatic scanning is selenium-75 labeled methionine. This agent has a high specificity for the pancreas and also the liver. Because of this affinity for both organs, a liver scan is obtained and then a pancreatic scan is obtained which includes both the pancreas and liver. One may then "subtract" the liver area and observe only the pancreas.

To date, many procedures using special medications, diets, and different scanning times have been utilized. The method currently being used requires that the patient be injected intravenously with ^{99m}Tc sulfide colloid and a liver scan performed on the gamma camera. The patient is then positioned with the left side of the body elevated (approximately 20° oblique angle) thereby separating the pancreas from the liver, since the liver will shift to the right.

A "baseline" view is obtained at the area of the pancreas, and the ^{75}Se is injected intravenously. Serial gamma camera pictures (10 minutes each) are obtained for a total time of 60 minutes.

III. RATIONALE

The head, body, and tail of the pancreas will usually be visualized. With our present technique, mass lesions are difficult to identify. Perhaps the best identification of abnormal pancreatic function is a lack of concentration of ^{75}Se methionine in the pancreas.

PLACENTAL SCANNING

I. INTRODUCTION

Bleeding, especially during the third trimester of pregnancy, presents a major problem in diagnosis. This bleeding may be due to the presence of placenta previa, which must be diagnosed prior to delivery. As with any highly vascularized organ, the placental blood pool can be delineated by radionuclide tagging of the patient's blood.

II. ISOTOPES UTILIZED

The best isotope that may be utilized is ^{99m}Tc labeled albuminate because it allows a scan to be obtained which readily shows the size and position of the placenta and requires no more than 30 minutes to complete. Technetium-99m results in a low radiation dose to the patient and fetus.

Another agent that may be used is radioiodine-131 human serum albumin. There is only minimal transfer of the albumin across the placental barrier to the fetal circulation. Within two hours prior to scanning, the patient should receive 10 drops SSKI (saturated solution potassium iodide) to block the uptake of iodine in the thyroid gland of the mother and fetus. The patient's uterus is divided into twelve equal areas by marking with a red wax pencil (3 areas laterally and 4 areas longitudinally). Serial 1-2 minute counts are obtained with a scintillation probe, positioning the probe exactly perpendicular to the table on which the patient is lying. Two counts are taken over each area and two counts are obtained over the xiphoid process. The count of each area is calculated as a percentage of the count over the xiphoid process, which is taken as the 100% reference point. These percentages are then plotted on a schematic diagram of the uterus and the resulting patterns of radioactivity are interpreted. The highest areas of concentration will usually indicate the position of the placental blood pool.

III. RATIONALE

Although other means of determining the presence of placenta previa are available, the isotopic method is considered to be preferable. For example, manual digital examination is considered inadvisable because of the possibility of gross hemorrhage. Roentgenologic procedures are also available, but the isotopic method of examination reduces the radiation exposure to both the mother and fetus.

SPLEEN SCANNING

I. INTRODUCTION

It is possible to visualize the spleen either with tagged red cells or colloids and thus show its location and morphology.

II. ISOTOPES UTILIZED

One technique of spleen scanning involves tagging the patient's red blood cells with chromium-51 (sodium chromate) and damaging the cells with heat. Once this has been accomplished, the red cells are reinjected into the patient and serial scans over the splenic area are performed after the spleen bed has concentrated the red cells. This method is technically difficult and if the red cells are not heat treated to exactly the proper temperature, the test is unsuccessful. With ^{99m}Tc sulfide colloid and ^{198}Au colloid, spleen scanning may be accomplished with ease. Both colloid materials have an affinity for the reticuloendothelial system of which the spleen is a part. The agent is injected intravenously and the scan may be initiated after a waiting period of approximately 15 minutes.

III. RATIONALE

The spleen may be enlarged by certain hematologic disorders, or liver diseases, or may rupture due to primary splenic trauma. It is first desirable to determine if the spleen is clinically palpable. If so, anterior and left lateral scans are obtained. If the spleen is not palpable, posterior and left lateral scans are obtained. These scans will show the splenic size, shape, and position. Clinically, the spleen is sometimes confused as being the left lobe of a very large liver. Since both ^{99m}Tc sulfide colloid and ^{198}Au colloid have a specific affinity for both spleen and liver, one anterior veiw will reveal the exact location of both organs, and by performing an iodine-131 rose bengal liver scan at a later date, one may use the "subtraction method" and obtain only the splenic area.

THYROID SCANNING

I. INTRODUCTION

The thyroid scan is an example of the use of a physiological mechanism to concentrate a radionuclide and make possible the visualization of the structure of an organ. This scan takes a relatively short period of time to perform (average--20-30 minutes), and even seriously ill patients can tolerate the procedure well.

II. ISOTOPES UTILIZED

The isotope is administered as sodium iodide in an oral liquid and metabolically follows the same pathway as normally occurring stable iodine (iodine-127). The iodine is ingested and is absorbed by the digestive tract in its inorganic form and circulated in the blood. The blood traverses the thyroid gland and under enzymatic control is selectively trapped by the thyroid cells in comparatively large amonts, i.e., the thyroid cell concentration is 20-30 times that of the blood concentration. Iodine-131 (sodium iodide) is the most commonly used isotope because of its availability, favorable shelf half-life and low dose.

Iodine-123 (sodium iodide) has been found to be a very valuable agent for thyroid scanning for several reasons. It provides two different energy ranges for scanning, 159 keV and 28 keV (x-ray range), the latter being particularly useful for suspected superficial "cold" nodules. For equivalent activities, the radiation dose to the thyroid gland from iodine-123 is less than that for iodine-131 by a factor of approximately 30.

III. RATIONALE

Size, shape, position, and the presence of "hot" or "cold" nodules of the thyroid gland can be accurately determined by the thyroid scan. Two techniques are commonly used. In "hand scanning" the collimated detector is placed over the selected sites and count rates are read and recorded from a ratemeter or a scaling circuit. In "automatic scanning," the detector moves mechanically in one or more planes and the counting rate is automatically recorded at selected times and spacings.

(a) Size - Knowing the size of the thyroid gland helps verify the clinical impression obtained on palpation and also to evaluate the gland size prior to radioiodine therapy.

(b) Shape - The shape of the thyroid gland is particularly noteworthy since there may be an agenesis of one lobe, one lobe may be larger than the other, surgical thyroidectomy may have been performed or a pyramidal lobe may be present. The thyroid scan is of particular benefit in determining the effectiveness or adequacy of the thyroidectomy and also when thyroid surgery is contemplated.

(c) Position - Determining the position of the thyroid gland by scan is helpful when substernal thyroid tissue, thyroglossal duct cyst or metastases of thyroid cancer are suspected.

(d) The presence of "cold" or "hot" nodules - A "hot" nodule of the thyroid gland infers hyperactivity. A single "cold" nodule (no activity or background activity) in the presence of normal functioning thyroid tissue must always be viewed with suspicion, e.g., a possible malignant nodule. Multiple "cold" nodules infer multinodular goiter.

The thyroid scan, along with the radioactive iodine uptake, gives an accurate method of diagnosing thyroid diseases and aids in their management.

EYE TUMOR LOCALIZATION

I. INTRODUCTION

The introduction of eye tumor localization by radioisotopic methods is useful, since it results in no trauma to the eye. It is not possible to biopsy intraocular lesions without loss of vision and destruction of the eye.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Phosphorus-32 as phosphate is utilized, since radiophosphorus uptake is greater in ocular tumors than in other areas of the eye. Since most intraocular tumors are located on the periphery of the eye, pure beta emitters, such as radiophosphorus, can be used for the localization. The patient is injected intravenously with the radiophosphorus and the tumor localization proceeds in 48 hours. Special eye tumor localization probes (usually Geiger-Mueller tubes) and count rates are accurately determined over multiple designated areas of each eye.

III. RATIONALE

This test will detect best those tumors which lie near the anterior segment of the eye because the tumor is more readily accessible for detection and also because the beta particles from phosphorus-32 can travel only a short distance, thus making detection of deeply placed tumors difficult. Increased localization of the isotope over the suspected area of the eye indicates disease. It is also possible to localize posterior lesions of the eye, but this procedure must be performed in surgery since it is necessary to position a small radiation detector behind the eye after incising the conjunctiva.

BLOOD VOLUME

I. INTRODUCTION

Using radioisotopic methods, it is possible to determine plasma volume, red blood cell mass and thus to calculate the blood volume and whole body hematocrit.

II. ISOTOPES UTILIZED AND APPROACH TO TECHNIQUE

The most precise method for determining the plasma volume and red cell mass is the simultaneous use of iodine-125 serum albumin (radioiodinated human serum albumin) for plasma volume determinations and ^{51}Cr (sodium chromate) for red cell mass. Iodine-125 is more commonly used because of its longer shelf life, it is less likely to liberate free iodide and allows simultaneous estimation of red cell mass with ^{51}Cr since their activities may be determined from the same sample by the gamma-ray spectrometer. Iodine-125 serum albumin is used because it mixes promptly with blood constitutents in about 10-30 minutes in a uniform manner, and, with serial sampling of the blood postinjection, the concentration of the activity in the plasma can be readily ascertained with suitable well type scintillation counters. With the use of ^{51}Cr (sodium chromate), however, an aliquot of the patient's blood must be procured and the red blood cells are tagged with the ^{51}Cr in vitro by a special procedure and then reinjected into the patient. Again, serial samples are obtained postinjection and the activity within the red cell aliquots is obtained. The energies of these two isotopes are sufficiently different to permit measurement of both in the same blood sample using proper instrumentation.

III. RATIONALE

From the procedure, the patient's plasma volume, red cell mass and whole body hematocrit may be determined. The patient's height and weight are obtained and by applying J. A. Retzloff's formulae (see appendix IV), one may ascertain the normal red cell mass and plasma volume for this particular patient. Some indications for this procedure are polycythemia, hemorrhage, anemia, cardiac or renal diseases of unknown etiology and as a pre-work-up where it is known that radical surgery will be performed.

RED BLOOD CELL MASS, SURVIVAL, AND SEQUESTRATION STUDIES

I. INTRODUCTION

The use of an agent which binds itself to the red blood cell and is not reutilized in production of the cells makes it possible to study red blood cell volume, gastrointestinal bleeding, survival time of the red cells and the organs of sequestration of red cells if it occurs.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Chromium-51 (sodium chromate) is the agent utilized for this technique. It is a particularly useful isotope in that it has a very favorable physical half-life of 27.8 days and its gamma emission can readily be detected with a scintillation counter. An aliquot of the patient's blood is obtained and the red cells are then tagged with the sodium chromate by a special procedure. It is then reinjected intravenously into the patient and serial blood samples are taken so that a red blood cell mass (in milliliters) determination may be obtained. As in the iron kinetic studies, external measurements with suitable equipment are made over the precordium, spleen, liver, and sacral areas to note areas of localization. Twenty-four hours postinjection of the ^{51}Cr tagged cells another blood sample is obtained and serial ones thereafter every two to three days for approximately 30 days to see how the tagged cells survive. If it is necessary for the patient to receive a blood transfusion during this period, the results are invalidated.

III. RATIONALE

Since the ^{51}Cr is bound to the red cells and not reutilized, the red blood cell life span may be determined by studying the decreasing radioactivity in the whole blood. A shortened life span of the red cell may be due to hemolytic anemia or bleeding. With the external measurements of radiation in the precordium, spleen, liver, and sacral areas, it is sometimes possible to detect the exact site of red cell sequestration and destruction, e.g., the spleen. A splenectomy may be indicated in this situation.

RENOGRAMS (KIDNEY FUNCTION TEST)

I. INTRODUCTION

The renogram is a quick method of appraising the function of each kidney separately, and is very useful in screening hypertensive patients to find those who may have surgically correctable unilateral renal disease. Incorporating this test result with blood chemistries and the I.V. pyelogram x-ray is often valuable in arriving at the proper diagnosis in renal diseases.

II. ISOTOPE UTILIZED AND APPROACH TO TECHNIQUE

Iodine-131 hippuran (orthoiodohippurate) is the agent employed. It is necessary that 10 drops of SSKI be administered three times the day prior to testing, in order to minimize the uptake of radioactive iodine in the thyroid gland. Also the exact location of the kidneys must be predetermined either by kidney localization techniques with isotopes, the I.V. pyelogram x-rays, or an x-ray film of the adbomen. The patient is placed in a prone position and a scintillation probe is placed directly over each kidney. The matched probes are connected to strip-chart recorders through ratemeters. Appropriate activity of the iodine-131 hippuran is injected rapidly intravenously and recordings of the passage of the isotope are made for a duration of at least 30 minutes over each kidney.

III. RATIONALE

Diagrammatically, three phases of kidney function are recognized. The first phase is thought to represent the arrival of the tracer bolus down the aorta and is seen even if the kidney is absent. The second and third phases represent the "secretory" function of the kidney plus drainage of urine via the collecting tubules, processes which occur virtually simultaneously. Mathematic computations together with overall pattern appearances are utilized to evaluate the renogram. Abnormal results indicate only that these are functional or structural differences between the two kidneys. Dehydration may give abnormal tracings. Indications for this test are renal dysfunction, hypertension, unilateral renal artery disease, suspected agenesis or renal obstructive uropathy.

APPENDIX I

MATHEMATICS REVIEW

I. INTRODUCTION

The nuclear medical technologist must be able to apply basic mathematical principles to practical situations. Mathematics is a valuable tool to help him perform his duties. The person who masters this tool can work more effectively and with far greater insight than someone who regards mathematics as an evil to be avoided. A working knowledge of elementary calculus is helpful, but not absolutely essential. The equivalent of a good background in college level algebra is generally considered the minimum requirement.

Presented here is a brief review of a few mathematical concepts which are particularly applicable to calculations frequently performed in nuclear medicine. Topics covered are exponents, large and small numbers, logarithms, and exponential functions.

II. EXPONENTS

In the expression $y = x^a$, x is called the "base" and a is the "exponent" designating the power to which the base is raised. When working with exponents, three fundamental laws must be observed:

1. THE PRODUCT OF ANY NUMBER OF FACTORS, EACH CONTAINING THE SAME BASE RAISED TO ANY POWER, IS EQUAL TO THE BASE RAISED TO THE SUM OF THE INDIVIDUAL EXPONENTS.

For example, if one wishes to evaluate the product, $2^2 \times 2^3 \times 2^2 = ?$, he may proceed in one of two ways: Each factor may be evaluated separately and the individual products multiplied:

$$2^2 = 2 \times 2 = 4$$

$$2^3 = 2 \times 2 \times 2 = 8$$

$$2^2 = 2 \times 2 = 4$$

Then,

$$4 \times 8 \times 4 = 128.$$

The same result may be obtained in one operation by adding the exponents:

$$2^2 \times 2^3 \times 2^2 = 2^{(2+3+2)} = 2^7 = 128.$$

The above stated law is written algebraically as:

$$x^a \cdot x^b \cdot x^c . . . x^n = x^{(a+b+c+. . .+n)}$$

2. THE QUOTIENT OF TWO TERMS, EACH CONTAINING THE SAME BASE RAISED TO ANY POWER, IS EQUAL TO THE BASE RAISED TO THE DIFFERENCE OF THE ALGEBRAIC SUM OF THE EXPONENTS IN THE NUMERATOR AND THE ALGEBRAIC SUM OF THE EXPONENTS IN THE DENOMINATOR.

Consider the quotient, $2^5 \div 2^3 = ?$

Evaluating the numerator and denominator separately yields

$$2^5 \div 2^3 = 32 \div 8 = 4$$

Applying the above rule, the same result is obtained by

$$2^5 \div 2^3 = 2^{(5-3)} = 2^2 = 4$$

The algebraic statement of this rule is:

$$x^a \div x^b = x^{a-b}$$

3. TO RAISE A TERM TO A POWER THAT CONTAINS A BASE RAISED TO A POWER, MULTIPLY THE EXPONENTS.

For example, suppose one wishes to evaluate the following: $(2^3)^2 = ?$

Evaluating the term in parentheses separately yields, $(2^3)^2 = 8^2 = 64$, or applying the rule directly, $(2^3)^2 = 2^{3\times 2} = 2^6 = 64$.

This rule is written algebraically as: $(x^a)^b = x^{a \times b}$

In addition to these three rules of exponents, one must also keep in mind that ANY BASE RAISED TO THE POWER ZERO IS NUMERICALLY EQUAL TO ONE. That is $x^0 = 1$ for all values of x except zero in which case, an absolute value is indeterminate.

III. LARGE AND SMALL NUMBERS

The nuclear medical technologist frequently performs calculations involving extremely large and small numbers. The preceding rules, with the number 10 as a base, greatly simplify these calculations. For instance, suppose one wished to evaluate: $(0.0000000875 \times 6340000000) \div (72000 \times 0.00000000067) = ?$

As it is written in decimal form, this calculation is extremely cumbersome. Since our numbering system is based on powers of 10 (i.e., using 10 as the base), the above numbers may be written as the desired number of significant figures times 10 raised to some power. Each movement of the decimal point changes the magnitude of the number by the factor 10. Thus, if we move the decimal point 6 places to the right, we increase the magnitude of the number by the factor 10^6. We multiply the number by 10^{-6} to compensate.

In this example, 0.0000000875 has seven zeros between the decimal point and the first significant figure. Thus, it may be written as 8.75×10^{-8} since the decimal point has been moved eight places to the right. Similarly, the number 6340000000 may be written as 6.34×10^9 by moving the decimal point nine places to the left. Continuing with the example, $72000 = 7.2 \times 10^4$ and $0.00000000067 = 6.7 \times 10^{-10}$.

Thus the quotient becomes

$$\frac{(8.75 \times 10^{-8})(6.34 \times 10^{9})}{(7.2 \times 10^{4})(6.7 \times 10^{-10})} = ?$$

Now only the significant figures need be multiplied and divided. The appropriate power of 10 is determined by using the previously stated rules of exponents.

Rewriting the example and solving yields:

$$\frac{(8.75)(6.34)}{(7.20)(6.70)} \left[\frac{10^{(-8+9)}}{10^{(4-10)}}\right] = 1.15 \quad \left[\frac{10^{1}}{10^{-6}}\right] = 1.15 \times 10^{7}$$

which may be written in decimal form as 11500000.

A quotient containing any number of factors may be evaluated in this way.

IV. LOGARITHMS

Consider the equation $y = a^x$ in which the base, a, is raised to the x power. This same equation may be written in the form, $\log_a y = x$. In the first statement, x is written as an exponent, while in the second, x is expressed as a logarithm. The latter expression states, "x is the logarithm of y if a is used as the base."

By comparing the two equations, one can deduce the general definition of a logarithm which states,"The logarithm of a number to any base is the power to which the base must be raised to give the number." Thus, logarithms and exponents are identical; the same rules apply to both. It is necessary that all logarithms used in a given operation be expressed relative to the same base. Almost any number could serve as a base, but only two are in common usage: common or Briggsian logarithms (base 10) and natural or Naperian logarithms (base e = 2.71828. . .). The choice of 10 as a base is obvious; our system of numbers is based on powers of 10. The significance of e may not be so readily apparent, and the reader is referred to any college algebra book for a discussion of the origin of e. The use of e as a base simplifies the mathematical statements of facts concerning quantities which are changing at a rate proportional to the magnitude of the quantity.

A. Rules for Using Logarithms

The following symbolism has been generally adopted and will be used throughout the remainder of this chapter:

$$\log_{10} x = \log x$$

$$\log_e x = \ln x$$

As previously mentioned, the rules for using logarithms are identical to those for exponents. Restated in logarithmic terms they are:

1. $\ln(a \cdot b \cdot c. \, . \, .n) = \ln a + \ln b + \ln c + \, . \, . \, . + \ln n$
2. $\ln \frac{a}{b} = \ln a - \ln b$
3. $\ln a^b = b \ln a$

In addition, two generalities should be kept in mind

4. The logarithm of any number to the same base as the number is one. That is, ln e = 1 and log 10 = 1.
5. The logarithm of 1 to any base is zero.

V. EXPONENTIAL FUNCTIONS

Many physical, chemical, and biological phenomena exhibit the property of changing, either naturally or by artificial means, at a rate proportional to the amount of a material present at any time. These processes are said to be "exponential" in their time rate of change, and the amount present at any time is proportional to the amount present at an earlier time multiplied by some power of e. Radioactive decay is an exponential relationship.

Some examples of exponential equations and their graphical presentation are given in the material which follows. The student should become familiar with these exponential relationships and practice evaluating them. Values of e raised to positive and negative powers are given in any good set of mathematical tables, or a slide rule may be used to evaluate this function.

In the three examples presented, the following symbol explanation applies.

A = amount present at time t

e = base of natural logarithms

k = exponent of e which determines rate of change (rate constant)

Δt = elapsed time

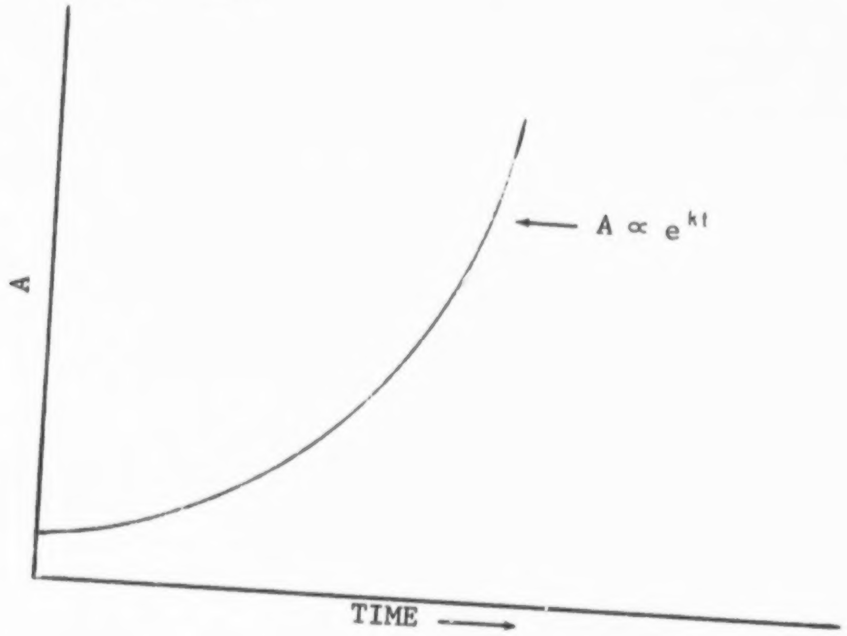

Figure I.--Curve Representing the Change in a Quantity which Increases Exponentially

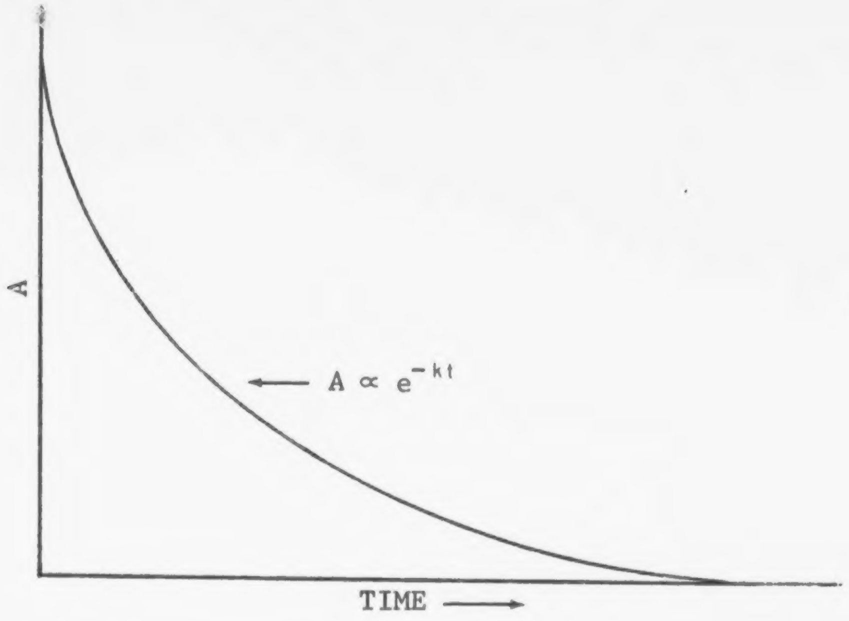

Figure 2.--Curve Representing the Exponential Decrease of a Quantity

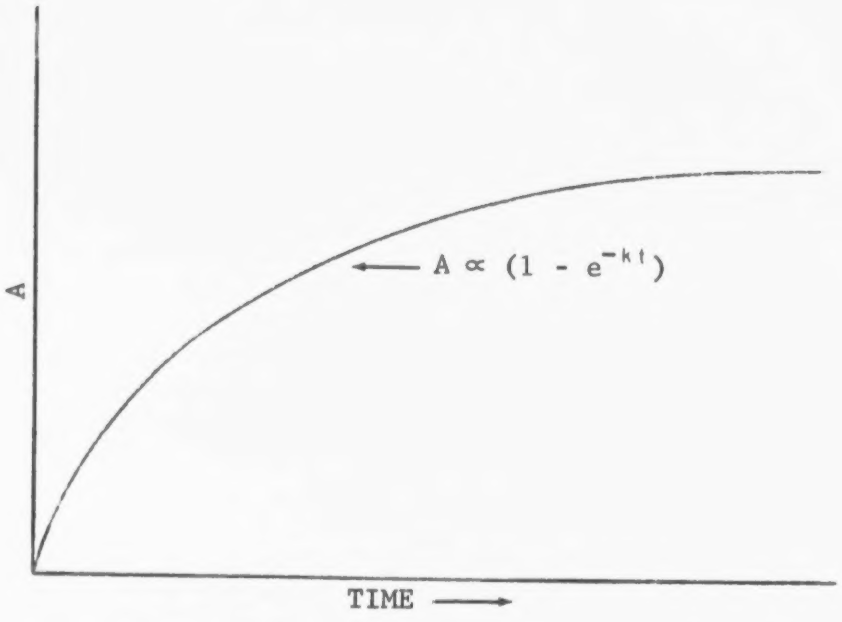

Figure 3.--Curve Representing the Change in a Quantity which Is Being Formed at a Constant Rate while it is Decreasing Exponentially

APPENDIX II

RADIONUCLIDE ACTIVITY SCHEDULE
FOR CLINICAL RADIOISOTOPE STUDIES

Adult Schedule

NUCLEAR MEDICINE DEPARTMENT
UNIVERSITY OF CINCINNATI MEDICAL CENTER

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Appendix II

Thyroid Diagnostic Procedures

Study	Radionuclide & Chemical Form	Activity Administered	Time Interval Before Testing
1. RAI Uptake	Iodine-131 or Iodine-123 Sodium Iodide	10 μCi orally	24 hours
2. Protein Bound Iodine Conversion Ratio	Iodine-131 Sodium Iodide	50 μCi orally	24 & 48 hours
3. Chromatography	Iodine-131 Sodium Iodide	100 μCi orally	Blood samples 48, 96 and 120 hours
4. TSH Uptake Study	Iodine-131 or Iodine-123	μCi administered = 50% above activity remaining in gland	24 hours
5. Thyroid scan	Iodine-131 or Iodine-123 Sodium Iodide	100 μCi orally	24 hours
6. T-3 Suppression Test (Cytomel Suppression)	Iodine-131 or Iodine-123 Sodium Iodine	μCi administered = 50% above activity remaining in gland	24 hours
7. T-3 Resin Test (*In Vitro*)	Iodine-131 Sodium Iodide		
8. RAI Uptake and Scan	Iodine-131 or Iodine-123 Sodium Iodide	100 μCi orally	24 hours

Metabolic Studies (Nonthyroid)

Study	Radionuclide & Chemical Form	Activity Administered	Time Interval Before Testing
1. Fats			
a. Triolein Test	Iodine-131 Triolein Glyceryl Trioleate	50 μCi orally	Blood samples 2,3,4,5,6, hours
b. Oleic Acid	Iodine-131 Oleic Acid	50 μCi orally	Blood samples 2,3,4,5,6, hours
2. Iron			
a. Absorption	Iron-59 Ferrous Citrate	1 μCi orally 700 μg. Ferrous Ammonium Sulfate 300 mg. Ascorbic Acid	Stool Samples × 7 days
b. Iron Binding Capacity Test	Iron-59 Ferrous Citrate	Test Performed In Vitro	———
c. Plasma Clearance and/or Turnover	Iron-59 Ferrous Citrate	20 μCi I.V.	Blood Samples 10,20,30,60, 90,120 and 180 minutes
d. RBC Uptake and/or Turnover	Iron-59 Ferrous Citrate	20 μCi I.V.	Periodic Blood Samples for 14 days
e. *In Vivo* Counting	Iron-59 Ferrous Citrate	20 μCi I.V.	Periodic Counting for 14 days
3. Protein			
a. Hypoproteinemia (Intestinal Loss)	Chromium-51 Albumin	50 μCi I.V.	Stool Samples × 4 days
	Iodine-125 Serum (human) Albumin	50 μCi I.V.	"
	Iodine-131 Serum (human) Albumin	10-50 μCi I.V.	"

Metabolic Studies (Non Thyroid)
(continued)

Study	Radionuclide & Chemical Form	Activity Administered	Time Interval Before Testing
4. Vitamins			
a. 1st Stage Schilling	Cobalt-57 Cobalt-60 Cyanocobalamin	0.5 µCi orally * 0.5 µCi orally	Urine Collection x 24 hrs. Urine Collection x 24 hrs.
b. 2nd Stage Schilling (with Intrinsic Factor)	Cobalt-57 Cobalt-60 Cyanocobalamin	0.5 µCi orally * 0.5 µCi orally	Urine Collection x 24 hrs. Urine Collection x 24 hrs.
c. 3rd Stage Schilling (Tetracycline x 7-10 days)	Cobalt-57 Cobalt-60 Cyanocobalamin	0.5 µCi orally * 0.5 µCi orally	Urine Collection x 24 hrs. Urine Collection x 24 hrs.

*1000 micrograms vitamin B-12 intramuscularly 2 hours post-administration of activity.

Scanning Procedures

Study	Radionuclide & Chemical Form	Activity Administered	Time Interval Before Testing
1. Bone	Strontium-85 Strontium Nitrate	1 µCi/kgm or 100 µCi I.V. (Bowel prep. prior to scan)	72 hours or longer
2. Brain	Technetium-99m Pertechnetate	15 mCi I.V. (age above 40)	20-30 minutes (not to exceed 3 hours)
		10 mCi I.V. (age 15-40)	
	Mercury-197 Chlormerodrin (Neohydrin)	1 mCi I.V. (1 ml. Mercuhydrin I.M. night before)	1 1/2 - 2 hours
	Mercury-203 Chlormerodrin (Neohydrin)	700 µCi I.V. (1 ml. Mercuhydrin I.M. night before)	1-1/2 - 2 hours
3. Mediastinum	Technetium-99m Albumin	10 mCi I.V.	Immediately
	Technetium-99m Pertechnetate	10 mCi I.V.	Immediately
	Iodine-131 Human Serum Albumin	100 µCi I.V.	45 minutes
4. Kidney	Mercury-197 Chlormerodrin (Neohydrin)	150 µCi I.V.	45 minutes

Scanning Procedures
(continued)

Study	Radionuclide & Chemical Form	Activity Administered	Time Interval Before Testing
5. Liver	Technetium-99m Sulfide Colloid	1 mCi I.V.	Immediately
	Iodine-131 Rose Bengal	150 µCi I.V.	10-15 minutes
	Gold-198 Colloid	150 µCi I.V.	10-15 minutes
6. Lung	Technetium-99m Macroaggregated Alb.	3 mCi I.V.	Immediately
	Iodine-131 Serum Alb. Macroaggregates	300 µCi I.V.	Immediately
7. Pancreas	Selenium-75 Selenomethionine	150-250 µCi I.V.	Immediately
8. Placenta	Iodine-131 Serum Alb. Serum Human Albumin	5 µCi I.V.	10 minutes
	Chromium-51 Sodium Chromate	10 µCi I.V.	10 minutes
	Technetium-99m Albuminate	1 mCi I.V.	Immediately
9. Spleen	Technetium-99m Sulfide Colloid	1 mCi I.V.	Immediately
	Chromium-51 Sodium Chromate	150-200 µCi I.V.	4 and 24 hours
	Gold-198 Colloid	100 µCi I.V.	10-15 minutes

Scanning Procedures
(continued)

Study	Radionuclide & Chemical Form	Activity Administered	Time Interval Before Testing
10. Thyroid	Iodine-131 or Iodine-123 Sodium Iodide	100 µCi orally	24 hours
11. Thyroid Cancer Work-Up (includes scans of neck, chest, and bone)	Iodine-131 or Iodine-123 Sodium Iodide	1-2 mCi orally	24 hours

Specialized Tumor Study

Study	Radionuclide & Chemical Form	Activity Administered	Time Interval Before Testing
1. Eye Tumor	Phosphorus-32 Sodium Phosphate	750 uCi I.V.	48 hours

Hemodynamic and Blood Studies

1. Hemodynamics (Circulation)			
a. Blood Vol. (Plasma Volume)	Iodine-125 Human Serum Albumin	20 μCi I.V.	10 and 20 minutes
	Iodine-131 Human Serum Albumin	5 μCi I.V.	10 minutes
b. Liver Blood Flow	Iodine-131 Rose Bengal	150 μCi I.V.	Immediately
c. Kidney Function	Iodine-131 Hippuran Sodium Iodohippurate	1 μCi/3.5 kgm. body weight I.V.	Immediately
2. Red Cell Studies			
a. Red Cell Mass	Chromium-51 Sodium Chromate	160 μCi I.V.	20 and 30 minutes
b. Red Cell Survival	Chromium-51 Sodium Chromate	160 μCi I.V.	Periodic counting up to one month*
c. In-Vivo Sequestration	Chromium-51 Sodium Chromate	160 μCi I.V.	Periodic counting up to one month*

*1,3,5,7,10,14,21 and 28 days.

APPENDIX III

Total Mean Radiation Dose to Standard Man From Administered Radioisotopes[1]

Organ or pool	Type of study	Radionuclide & Chemical form	Route	Mean dose to standard man[2] (mrad per μCi administered)						
				Whole Body	Blood	Bone Marrow	Kidney	Liver	Spleen	Thyroid
Thyroid gland	Uptake	Iodine-131 Sodium iodide	oral	0.4						1500
	Scan	Iodine-131 Sodium iodide	oral	0.4						1500
		Technetium-99m Pertechnetate	I.V.	0.01						0.3
Ferro-kinetics	Iron absorption	Iron-59 Ferrous citrate	oral							
		Iron-59 Ferric chloride	oral	3					15	
	Plasma iron transport, degree, and site of erythropoiesis	Iron-59 Ferrous citrate	I.V.							
		Iron-59 Ferric chloride	I.V.	20						
Circulatory system	Liver blood flow	Gold-198 Colloidal gold	I.V.	2		4		40	40	
	Placental localization	Iodine-131 Serum albumin	I.V.	2	20					1

APPENDIX III (continued)

Organ or pool	Type of study	Radionuclide & Chemical form	Route	Mean dose to standard man[2] (mrad per μCi administered)						
				Whole Body	Blood	Bone Marrow	Kidney	Liver	Spleen	Thyroid
Circulatory system	Placental localization (continued)	Chromium-51 Tagged RBC	I.V.	0.3	2					
		Technetium-99m Albumin	I.V.	0.02	0.05					
Blood	Plasma volume	Iodine-131 Serum albumin	I.V.	2	20					1.0
		Chromium-51 Serum albumin	I.V.	0.2	2					
	Red cell volume & survival	Chromium-51 Tagged RBC	I.V.	0.3	2				40	
Spleen	Scan	Chromium-51 Tagged RBC	I.V.	0.3	2				40	
Skin, visible mucous membranes, cavity linings, eye	Tumor diagnosis, localization	Phosphorus-32 Disodium phosphate	I.V.	8		40		30	30	
Brain	Scan, tumor localization	Mercury-203 Chlormerodrin	I.V.	0.4			80			
		Mercury-197 Chlormerodrin	I.V.	0.1			5			
		Iodine-131 Serum albumin	I.V.	2	20					
		Technetium-99m Pertechnetate	I.V.	0.01						0.1 (thyroid blocked)

APPENDIX III (continued)

Organ or pool	Type of study	Radionuclide & Chemical form	Route	Mean dose to standard man[2] (mrad per μCi administered)						
				Whole Body	Blood	Bone Marrow	Kidney	Liver	Spleen	Thyroid
Liver	Scan, tumor localization, structure	Iodine-131 Rose Bengal	I.V.	0.4						
		Gold-198 Colloidal gold	I.V.	2		4		40	40	
		Technetium-99m Colloidal sulfide	I.V.	0.02		0.02		0.3	0.3	
	Function	Iodine-131 Rose Bengal	I.V.	0.4						
Kidney	Scan	Mercury-203 Chlormerodrin	I.V.	0.4			80			
		Mercury-197 Chlormerodrin	I.V.	0.1			5			
	Function	Iodine-131 Hippuran	I.V.	0.03			0.6			
Absorption Studies	Vitamin B^{12}	Cobalt-57 Vitamin B^{12}	oral	5				80		
		Cobalt-60 Vitamin B^{12}	oral	200				5000		
	Fat	Iodine-131 Triolein or Oleic acid	oral	0.6						

APPENDIX III (continued)

Organ or pool	Type of study	Radionuclide & Chemical form	Route	Mean dose to standard man[2] (mrad per μCi administered)						
				Whole Body	Blood	Bone Marrow	Kidney	Liver	Spleen	Thyroid
Bone	Tumor localization	Strontium-85 Strontium chloride	I.V.		10					

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[1] The entries of the first four columns are based on tables given in the following reference: Silver,S., Nucleonics 23, (8), 106 (1965).

[a] There is no general agreement on the biological assumptions that are the basis of internal dose computations and therefore the published dose values vary significantly. The mean radiation doses given in the last seven columns are based on the following references: Osborn, S.B., and Ellis, R.E., in The Science of Ionizing Radiation (E. E. Etter, ed.), Chap. 29, Charles C Thomas, Springfield, 1965. Seltzer, R.A., Kereiakes, J.G., and Saenger, E.L., New Eng. J. Med. 271:84(1964). Smith, E. M., J. Nucl. Med. 6:231, (1965).

APPENDIX IV

ESTIMATION OF ERYTHROCYTE AND PLASMA VOLUME ACCORDING TO HEIGHT AND BODY WEIGHT

Formulas for Men:

Erythrocyte volume (ml) =
8.2 × height (cms) + 17.3 × weight (kgm) - 693 ± 252 ml (1 S.D.)

Plasma volume (ml) =
23.7 × height (cms) + 9 × weight (kgm) - 1709 ± 358 ml (1 S.D.)

Formulas for Women:

Erythrocyte volume (ml) =
16.4 × height (cms) + 5.7 × weight (kgm) - 1649 ± 129 ml (1 S.D.)

Plasma volume (ml) =
40.5 × height (cms) + 8.4 × weight (kgm) - 4811 ± 196 ml (1 S.D.)

Ref: J. A. Retzloff, Red Cell Volume, Plasma Volume and Lean Body Mass in Health Men and Women, The Development of a Blood Volume Standard, Thesis, Mayo Graduate School of Medicine, University of Minnesota, 1963.

WEIGHT FACTORS

		Males		Females	
Weight	Weight Kilograms	V_{RBC} 17.3(Wt.)	V_P 9.0(Wt.)	V_{RBC} 5.7(Wt.)	V_P 8.4(Wt.)
100 lbs.	45.5 kg.	787 ml.	409 ml.	259 ml.	382 ml.
101	45.9	794	413	262	385
102	46.4	803	418	264	390
103	46.8	810	421	267	393
104	47.3	818	426	270	397
105	47.7	825	429	272	401
106	48.2	834	434	275	405
107	48.6	841	437	277	408
108	49.1	849	442	280	412
109	49.5	856	445	282	416
110	50.0	865	450	285	420
111	50.5	874	454	288	424
112	50.9	880	458	290	427
113	51.4	889	463	293	432
114	51.8	896	466	295	435
115	52.3	905	471	298	439
116	52.7	912	474	300	443
117	53.2	920	478	303	447
118	53.6	927	482	305	450
119	54.1	936	487	308	454
120	54.5	943	490	311	458
121	55.0	951	495	313	462
122	55.5	960	499	316	466
123	55.9	967	503	319	469
124	56.4	976	508	321	474
125	56.8	983	511	324	477
126	57.3	991	516	327	481
127	57.7	998	519	329	485
128	58.2	1007	524	332	489
129	58.6	1014	527	334	492
130	59.1	1022	532	337	496
131	59.5	1029	535	339	500
132	60.0	1038	540	342	504
133	60.5	1047	544	345	508
134	60.9	1053	548	347	511
135	61.4	1062	553	350	516
136	61.8	1069	556	352	519
137	62.3	1078	561	355	523
138	62.7	1085	564	357	527
139	63.2	1093	569	360	531
140	63.6	1100	572	362	534
141	64.1	1109	577	365	538
142	64.5	1116	580	368	542

WEIGHT FACTORS

		Males		Females	
Weight	Weight Kilograms	V_{RBC} 17.3(Wt.)	V_P 9.0(Wt.)	V_{RBC} 5.7(Wt.)	V_P 8.4(Wt.)
143	65.0	1124	585	370	546
144	65.5	1133	589	373	550
145	65.9	1140	593	376	553
146 lbs.	66.4 kg.	1149 ml.	598 ml.	378 ml.	558 ml.
147	66.8	1156	601	381	561
148	67.3	1164	606	384	565
149	67.7	1171	609	386	569
150	68.2	1180	614	389	573
151	68.6	1187	617	391	576
152	69.1	1195	622	394	580
153	69.5	1202	625	396	584
154	70.0	1211	630	399	588
155	70.5	1220	634	402	592
156	70.9	1226	638	404	595
157	71.4	1235	643	407	600
158	71.8	1242	646	409	603
159	72.3	1251	651	412	607
160	72.7	1258	654	414	611
161	73.2	1266	659	417	615
162	73.6	1273	662	419	618
163	74.1	1282	667	422	622
164	74.5	1289	670	425	626
165	75.0	1297	675	427	630
166	75.5	1306	679	430	634
167	75.9	1313	683	433	637
168	76.4	1322	688	435	642
169	76.8	1329	691	438	645
170	77.3	1337	696	441	649
171	77.7	1344	699	443	653
172	78.2	1353	704	446	657
173	78.6	1360	707	448	660
174	79.1	1368	712	451	664
175	79.5	1375	715	453	668
176	80.0	1384	720	456	672
177	80.5	1393	724	459	676
178	80.9	1399	728	461	679
179	81.4	1408	733	464	684
180	81.8	1415	736	466	687
181	82.3	1424	741	469	691
182	82.7	1431	744	471	695
183	83.2	1439	749	474	699
184	83.6	1446	752	476	702
185	84.1	1455	757	479	706

WEIGHT FACTORS

		Males		Females	
Weight	Weight Kilograms	V_{RBC} 17.3(Wt.)	V_P 9.0(Wt.)	V_{RBC} 5.7(Wt.)	V_P 8.4(Wt.)
186	84.5	1462	760	482	710
187	85.0	1470	765	484	714
188	85.5	1479	769	487	718
189	85.9	1486	773	490	721
190	86.4	1495	778	492	726
191 lbs.	86.8 kg.	1501 ml.	781 ml.	495 ml.	729 ml.
192	87.3	1510	786	498	733
193	87.7	1517	789	500	737
194	88.2	1526	794	503	741
195	88.6	1533	797	505	744
196	89.1	1541	802	508	748
197	89.5	1548	805	510	752
198	90.0	1557	810	513	756
199	90.5	1566	814	516	760
200	90.9	1572	818	518	763

HEIGHT FACTORS

		Males		Females	
Height ft. in.	Height Centimeter	V_{RBC} (8.2)Ht.	V_P (23.7)Ht.	V_{RBC} (16.4)Ht.	V_P (40.5)Ht.
5 - 0 "	152	1246 ml.	3602 ml.	2493 ml.	6156 ml.
5 - ½ "	154	1263	3650	2526	6237
5 - 1 "	155	1271	3673	2542	6277
5 - 1½"	156	1279	3697	2558	6318
5 - 2 "	157	1287	3721	2575	6358
5 - 2½"	159	1304	3768	2608	6439
5 - 3 "	160	1313	3792	2624	6480
5 - 3½"	161	1320	3816	2640	6520
5 - 4 "	163	1337	3863	2673	6601
5 - 4½"	164	1345	3887	2690	6642
5 - 5 "	165	1352	3910	2706	6682
5 - 5½"	166	1361	3934	2722	6723
5 - 6 "	168	1378	3982	2755	6804
5 - 6½"	169	1386	4005	2772	6844
5 - 7 "	170	1394	4029	2788	6885
5 - 7½"	171	1402	4053	2804	6925
5 - 8 "	173	1419	4100	2837	7006
5 - 8½"	174	1427	4124	2854	7047
5 - 9 "	175	1435	4147	2870	7087
5 - 9½"	177	1451	4195	2903	7168
5 - 10"	178	1460	4219	2919	7209
5 - 10½"	179	1468	4243	2936	7249
5 - 11 "	180	1476	4266	2952	7290
5 - 11½"	182	1492	4293	2985	7371
6 - 0 "	183	1501	4337	3001	7411
6 - ½ "	184	1509	4361	3018	7452
6 - 1 "	185	1517	4384	3034	7492
6 - 1½ "	187	1533	4432	3067	7573
6 - 2 "	188	1542	4456	3083	7614
6 - 2½"	189	1550	4479	3100	7654
6 - 3 "	191	1566	4527	3132	7735
6 - 3½"	192	1574	4550	3149	7776
6 - 4 "	193	1583	4574	3165	7816
6 - 4½"	194	1591	4598	3202	7857
6 - 5 "	196	1607	4646	3214	7938
6 - 5½"	197	1615	4669	3231	7978
6 - 6 "	198	1624	4693	3247	8019

TECHNICAL REPORTS

(continued from inside of front cover)

MORP 68-9	Development and Evaluation of an Automatic Collimator for Medical Diagnostic X-ray Machines (PB 180 528)
MORP 68-10	Survey of the Use of Radionuclides in Medicine: Preliminary Report (Superseded by BRH/DMRE 70-1)
MORP 68-11	Dental Surpak Summary Report (PB 184 356)
MORP 68-12	Particle Accelerator Safety Manual (Supt. of Doc., GPO $1.25) (PB 178 325)
MORP 68-13	PHS Film Badge Program (In preparation)
MORP 68-14	Radiation Safety Recommendations for X-ray Diffraction and Spectrographic Equipment (PB 182 558)
DMRE 69-1	Report of the Task Force on X-ray Image Analysis and Systems Development (PB 184 130)
DMRE 69-2	Symposium on Past, Present, and Future State X-ray Programs (PB 184 481)
DMRE 69-3	Medical Radiation Information for Litigation (PB 187 697)
BRH/DMRE 70-1	Survey of the Use of Radionuclides in Medicine (PB 188 619)
BRH/DMRE C70-2	Automatic Data Processing System Study for Massachusetts General Hospital Diagnostic Radiology Department (PB 193 937)